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Improving Patient Safety Through Medical Device Regulation

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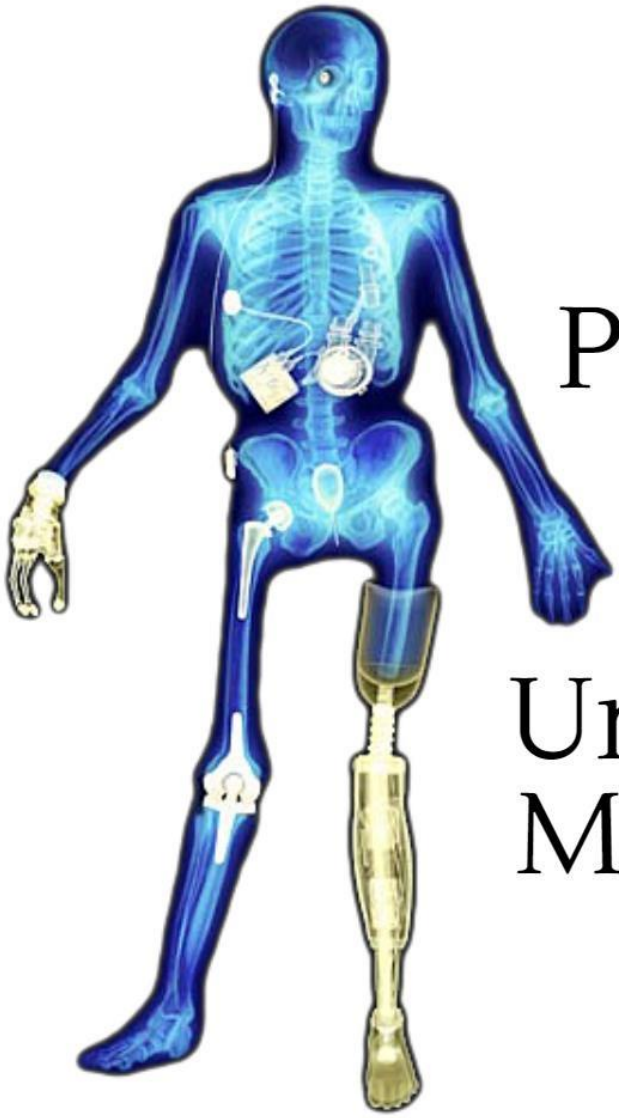

Improving Patient Safety in the European Union Through Medical Device Legislation

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Forbrugerrådet Tænk

Danish Consumer Council

Improving Patient Safety in the European Union Through Medical Device Regulation

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Project Sponsor:

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Danish Consumer Council

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Abstract

Recent concern has arisen over multi-national medical device manufacturers using European patients as metaphorical guinea pigs for testing their devices before seeking approval in stricter regulatory environments. We worked with the Danish Consumer Council to recommend changes to European Union medical device regulation that should help improve patient safety without stifling innovation. We gathered public opinion regarding medical device safety through a survey, and conducted in-depth interviews with key stakeholders. Our end result is a set of proposed reforms to the current EU regulations, including increasing transparency and requiring more clinical trials. Our sponsor will use these recommendations in policy discussion to influence legislation that will increase patient safety.

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Executive Summary

Project Scope

The European Union (EU) has a population of 503 million across 28 member states and is the second largest medical device market in the world. It approves new medical devices 2-3 years before they become available in US markets, due to its less restrictive regulatory policies (Boutrand, 2013). However, concerns have been raised that European patients are functioning as guinea pigs for countries with more robust regulatory systems (BEUC, July 2012). The goal of this project was to develop recommendations for changes to EU medical device regulation, specifically to accomplish two things: improve patient safety and maintain the current state of innovation in the EU medical device industry.

We worked to develop these recommendations together with Forbrugerrådet (FBR), a Danish non-governmental organization which advocates for consumer rights. These recommendations and the supporting data will be used by FBR to campaign for regulatory changes that will increase patient safety.

We used a variety of methods to come to our conclusions. Our aim was to get input from as many different perspectives as possible. To that end, we included some questions related to medical devices in a general survey that FBR sent out to its consumer panel (with over 1000 respondents) to get the general public's perspective, and we conducted interviews with representatives from the medical device industry and the European Parliament as well as doctors and regulatory authorities. Combined with our background research into the regulatory, legislative, and industrial perspectives, these methods ensured that as many relevant stakeholders as possible had a say in the content of our recommendations.

EU Medical Device Regulation

The primary goal of medical devices is to improve patient's lives; however, over the past few years, several medical devices used in the European Union have proven detrimental to patient health. Without a proper regulatory framework surrounding the medical industry, medical devices, procedures, and hospitals themselves expose patients to an unacceptably high level of risk. Under regulating high risk devices allows profit-driven industries to rush new devices to market before their safety and success rates can be sufficiently evaluated. On the other hand, over-regulation introduces an entry barrier to the medical device industry and drives up

development and production costs of new devices, effectively making them too expensive for companies to pursue. A balance must be reached between overly lenient and overly stringent regulation.

Denmark's government is quite aware of this delicate balance. While the Danish government clearly has a responsibility to protect its citizens, it also wants to preserve its country's strong international position in the health care industry. The Danish government's 2013 report "Denmark at Work" expressed Denmark's vision to become an attractive option for the development and manufacture of innovative healthcare solutions by offering a supportive environment for public-private collaboration, as well as fast implementation of new technologies. This vision requires a compromise between industry desires for more lenient laws, and patients' need for stricter ones. As the main consumer representation group in Denmark, FBR has become quite involved in the debate over what changes, if any, should be made to the current EU legislation and regulations.

In the current regulatory system in Europe, medical devices are approved by private companies called *notified bodies*, which are funded by review fees from manufacturers. These notified bodies are supervised by national agencies called *competent authorities*. After a device is approved, it must be monitored by the competent authority based on reports submitted by users (doctors and patients). If any problems arise, either the competent authorities or the manufacturer can take corrective action or issue a recall if necessary.

Problems and Solutions

We have identified many problems in the EU's medical device approval process in italics, which will be outlined in this section. Through our research, we have established solutions to these problems which are stated in this section in bold.

Standards are an integral and necessary part of the medical device approval process, but are currently written primarily by industry representatives

The medical device industry in the European Union is regulated by three directives for different types of devices. The directives outline many *essential requirements* that every device must meet to ensure it is safe and effective. Rather than outlining these requirements in a large amount of detail, they are deliberately left vague. Manufacturers are expected to use standards to

ensure that devices meet the essential requirements, since standards can be updated more quickly than legislation to reflect current technology. Notified bodies are then expected to check that the manufacturers follow those standards. The major problem with these standards is that they are written almost exclusively by industry representatives. In addition to missing important perspectives, this has also led to distrust of the standards by EU authorities. To remedy this problem, the clear solution is to **diversify representation on standards committees by including doctors, patients and regulators**. Due to the associated costs, this would require government subsidization, but the investment would pay off in increased safety and innovation, as standards allow manufacturers to avoid the costs and hazards of developing their own testing criteria.

There are too many notified bodies which vary too widely in their standards for device approval

The manner in which the notified body system currently operates is also problematic. The high number of notified bodies nearly guarantees that they will request differing amounts of evidence. The number of notified bodies varies between countries, ranging from too many for the competent authority to monitor well to only one, which many countries would be reluctant to punish too harshly and potentially put out of business. Finally, notified bodies are paid by manufacturers to approve their devices, which gives the notified bodies an incentive to approve more devices and therefore become a more attractive option than their competitors, as manufacturers can choose any notified body to approve their products. One option would be to create a central approval system, but due to widespread concerns about creating an inefficient bureaucratic process, this solution is not feasible. Rather, the best option seems to be **using a central authority to audit notified bodies and reduce their number by shutting down the most flawed ones**. This would also serve as a warning to other notified bodies to keep their standards high.

There is currently much debate about whether full clinical trials or reviews of similar devices are appropriate for most devices

Creating a central authority and reducing the number of notified bodies should make the evidence that notified bodies request more consistent. However, under the current system, they still have too much discretion in the type of data they require, and whether it needs to involve

human clinical trials. Most industry representatives approve of the current system, and believe that clinical trials are unnecessary and ineffective for most devices. At most, they would approve of a slight tightening of the requirements for approval, which could lead to more clinical trials but would not mandate them. On the other hand, a doctor we interviewed strongly emphasized the need for more clinical trials to prevent some of the more dramatic device failures that have occurred. Therefore, our recommendations need to balance these two viewpoints. The best option here is to **set a strong but not burdensome base: all new devices would require a phase II trial (20-150 subjects, looking at safety and effectiveness), while devices with very similar predicates would require a phase I trial (15-30 subjects, primarily focused on safety)**. To maintain flexibility, notified bodies would be able to request more data in the form of a longer or larger trial. Competent authorities could also grant exemptions, for example for a very ill patient to use a device still going through trials, or for a manufacturer to produce a device for a very rare condition without a full clinical trial.

The relationships between medical device manufacturers and doctors present a conflict of interest

After a device is approved, some companies will try to influence doctors into choosing their devices. There have even been cases in which doctors have received money from companies to promote their devices. Denmark recently passed laws to curb these types of abuses. Under these laws, gifts from manufacturers and compensation for professional activities must not exceed a specified monetary value. **We recommend that such laws be adopted EU-wide so that doctors can make objective decisions that are in their patients' best interests**.

There is a lack of transparency in the European medical device industry in device approval and post-market surveillance

Part of the problem with these relationships is that doctors must rely on manufacturers because information on medical devices is not available elsewhere. The EU does have a database called EUDAMED (EUropean DAtabank on MEdical Devices) that is supposed to contain a large amount of information on every device approved for use in the EU. However, access is limited to a very small group of people, and in part due to this, much of the information that should be present has never been uploaded to the database. Most of our interviewees mentioned

transparency, and all agreed that they would like to see greater transparency. We recommend **opening the information in EUDAMED up to the public, as well as creating a registry of all devices currently going through the approval process**. This registry would be open to authorities, notified bodies, and manufacturers to provide information to relevant parties, and to ensure that a device that failed to obtain approval from one notified body cannot be immediately sent to another.

Procedural complications are being reported at unacceptably low rates

To make the newly opened database useful, the amount of information in it also needs to be increased. Currently, many problems with medical devices in Denmark are never reported by doctors or patients, and even those that are fall prey to the country's fragmented reporting system. Denmark has three separate agencies that collect some form of reports. Due to the separate agencies and the separate databases each one maintains, no one has access to all the data on problems with medical devices. Additionally, despite the legal requirement to do so, many doctors do not report complications (*adverse events)*, whether due to lack of knowledge or reluctance to admit possible mistakes. Since doctors should not receive incentives to perform a part of their job, **a punitive system involving fines for doctors who do not report events would be a preferable option**. Additionally, **all the reports that come into any of the three agencies should be anonymized and placed into a central database, preferably EUDAMED**. This would make all the information available for analysis and allow Sundhedsstyrelsen (the Danish competent authority), as the only agency with the power to do so, to take corrective action or issue a recall if needed.

Patients are unaware of the risks involved with medical devices since information on the safety and efficacy of medical devices is not available to the general public

To make this information truly useful for patients, it needs to be condensed and presented to patients before they agree to undergo any procedure. Under the current system, doctors are supposed to present information to patients, but what information and how much is left to their discretion, so patients could receive any amount of information. To remedy this situation, **we recommend that the information patients receive be subject to regulation**. All patients should receive enough information to be fully informed of the potential risks and benefits of their

procedure. This information should also be presented in a form and at a level where it is intelligible to a layperson in 15 minutes. Additionally, in the event of a post-market device failure, there are a wide variety of people and agencies to which the patient can turn. This can potentially be overwhelming to a patient. Therefore, **we recommend setting up a phone number that patients can call and be directed to the appropriate agency, depending on their issue**. This would also increase the number of reports going to the central database, providing a better view of the overall post-market performance of medical devices. See Figure 1 for a chart summarizing our recommendations.

Conclusion

Overall, these recommendations are designed to improve patient safety without stifling innovation. Legislation is not simple to change to begin with, and the controversial nature of medical device regulation only increases the difficulty. The current proposals for change in the European Parliament have been debated for several years and are still awaiting a vote. There are many sides to the issue, and it is a complicated matter to arrive at an agreement acceptable to all the relevant stakeholders. We believe our project has brought new voices to the table, sought to understand the established perspectives, and synthesized them from an outsider's point of view. In our recommendations we have endeavored to provide a compromise, and we hope that, in the future, our recommendations will bring change that ultimately makes patients safer.

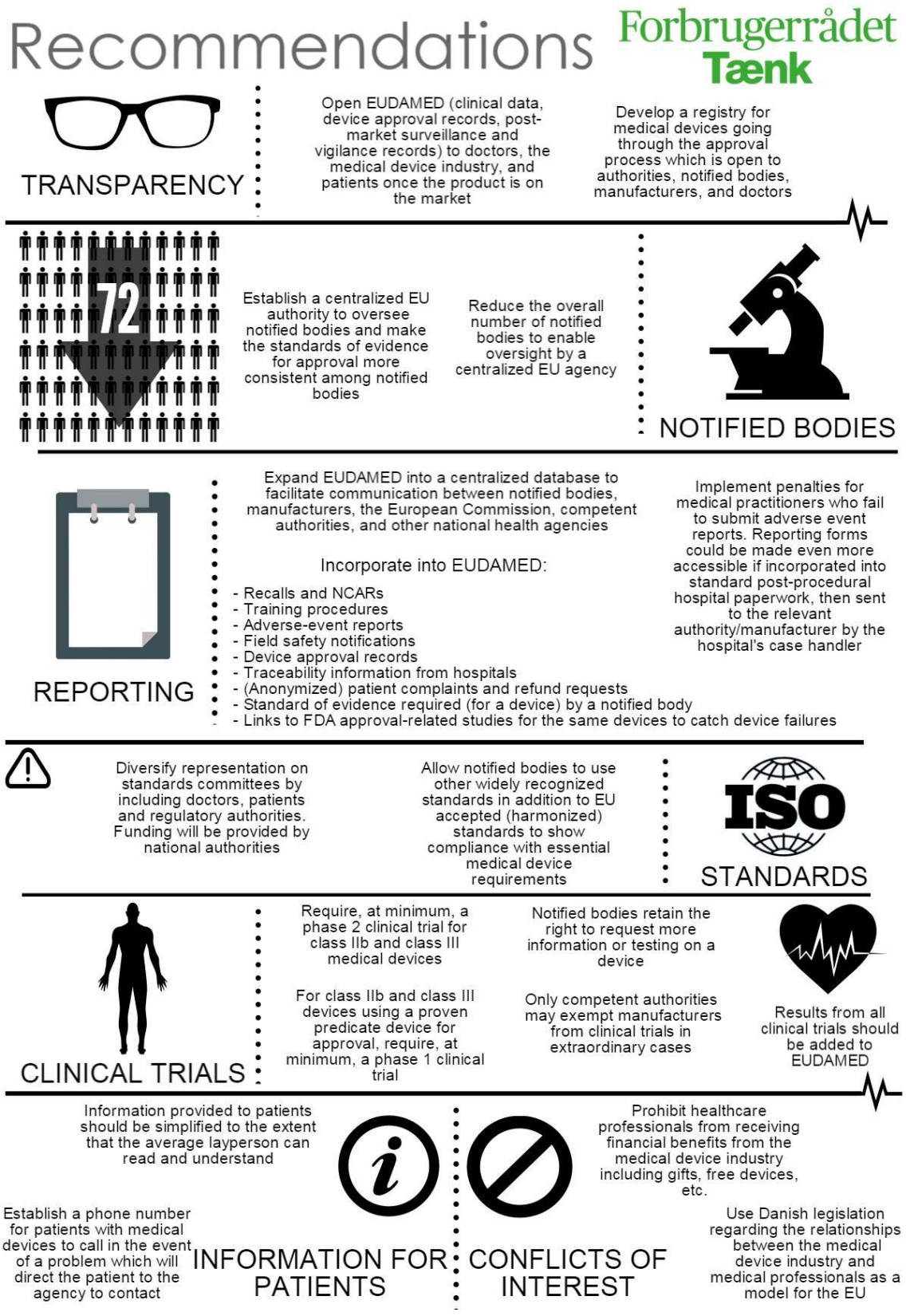

Figure 1. Recommendations Chart (Sam Jacobs, 2015)

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Chapter 1: Introduction

The primary goal of medical devices, as a component of health care, is to improve the health of the patients on whom they are used, and regulations must reflect this goal. However, over the past few years, several medical devices used in the European Union (EU) have proven detrimental to patient health. Poly Implant Prothèse (PIP), a French company, manufactured breast implants over a nine year period that were later found to be manufactured from industrial grade, rather than medical grade, silicone. This made them more likely to rupture, with a 25-30% 10-year failure rate; the ruptures caused inflammation and irritation within and around the breast tissue (European Commission SCENIHR, 2013). Additionally, several brands of large-diameter metal-on-metal hip implants were produced by various companies. These implants were later discovered to release metal ions into the bloodstream, destroying bone and muscle tissue, and were more likely to fail altogether (Cohen, February 2012). Unsafe medical devices that gained European approval such as these have drawn attention to the need for regulatory changes in the EU.

Without a proper regulatory framework surrounding the medical industry, medical devices, procedures, and hospitals themselves expose patients to an unacceptably high level of risk. Under regulating high-risk devices allows profit-driven industries to rush new devices to market before their safety and success rates can be sufficiently evaluated. On the other hand, over-regulation introduces an entry barrier to the medical device industry and drives up development and production costs of new devices, effectively making them too expensive for companies to pursue. In this way, over-regulation stifles innovation in the medical device industry. The looser regulations in the EU provide European patients with earlier access to innovative yet unproven, high-risk, high-reward medical devices and procedures. The dangers associated with these devices are unknown, and present a risk to the patients. However, European patients with limited treatment options gain the opportunity to undergo potentially lifesaving medical procedures.

The EU, the second largest medical device market in the world, approves new medical devices 2-3 years before they become available in US markets, due to its less restrictive regulatory policies (Boutrand, 2013). Figure 1.1 shows the average monthly approval delays for premarket approval of medical devices in the US from 2004 to 2010. The US regulatory system requires the additional time because medical device companies need to gather data from clinical

trials on the device in order to obtain premarket approval (Kaplan et al., 2004). It is generally recognized that the United States' regulatory system is very strict; as a result American manufacturers have been gaining approval on their devices in the EU before seeking the clinical trial data mandated for FDA approval. In this manner, EU directives are essentially allowing foreign companies to use European patients as metaphorical guinea pigs for their largely unproven medical devices.

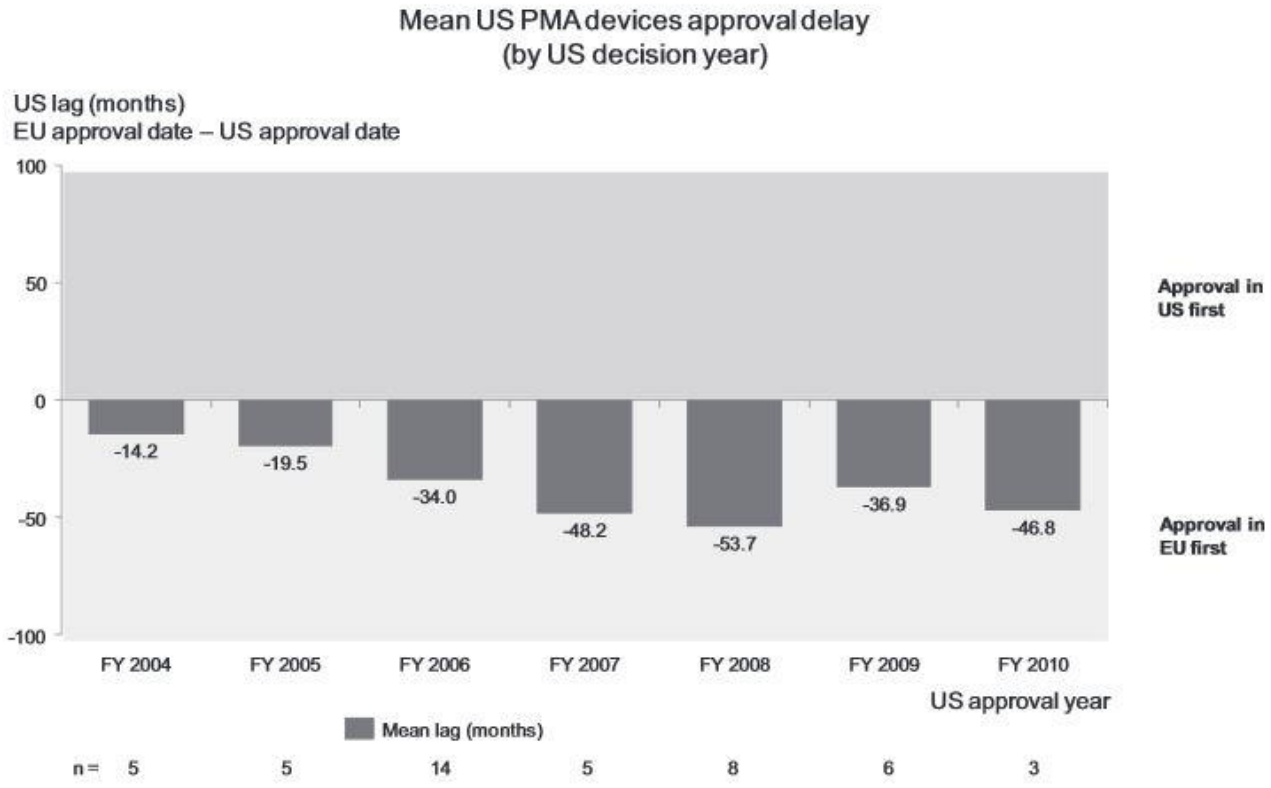

Figure 1.1 The average delay of medical device approval in the US compared to the EU (California Healthcare Institute & The Boston Consulting Group, Feb. 2011)

Changes to EU directives affect all 28 member states and their citizens, and therefore cannot be taken lightly. Different organizations have advanced proposals for the types of regulatory changes they would like to see, both specific items and broader, structural changes. There are currently two medical device proposals under consideration in the European Parliament. These proposals are indicative of the direction in which medical device legislation is moving in the EU and highlight some important issues with the current regulatory system.

While the proposals have been repeatedly postponed due to continual debate and compromise amendments, there are other organizations which are investigating regulatory reform from different perspectives. The Danish Consumer Council, Forbrugerrådet (FBR), is a non-governmental organization which advocates for consumer rights. We worked with FBR to develop recommendations for changes to EU medical device regulation. These recommendations and the supporting data will be used by FBR's senior health officer, Sine Jensen, to campaign for regulatory changes that will increase patient safety. While our recommendations overlap to some extent with those of the proposals currently in the European Parliament, we also developed some new recommendations. For instance, we determined that all patients should be given sufficient information on medical devices before they undergo a medical procedure and that representation in standards committees should be more diverse.

In our recommendations overall, we endeavored to improve patient safety while accounting for medical device industry, healthcare industry, and regulatory perspectives. All the involved parties we were able to contact have had a say in their content. The background chapter covers some of these perspectives in more detail as well as giving some more general background information about the regulatory process. It also compares the current state of the regulatory system in the EU with that of the US. In chapter 3, we cover our methodology for the project, including our goal and objectives. Chapter 4 lays out our findings and recommendations for changes to medical device regulation.

Chapter 2: Background

Over the past few years, the European Union (EU) has suffered from a number of scandals involving unsafe medical devices. The term medical device represents a broad category that includes any non-drug piece of equipment used in health care, from a Band-Aid to an implantable heart pump or MRI machine. One of the largest scandals involved Poly Implant Prothèse (PIP) breast implants, which were used in 300,000 women before they were discovered to be made from industrial-grade instead of medical-grade silicone. The extra impurities found in the industrial-grade silicone made the implants more likely to rupture, leaking the gel inside the implants into the body and causing irritation and inflammation (European Commission SCENIHR, 2013). Another scandal involved metal-on-metal hip implants, a type of hip implant in which the parts corresponding to the thigh and pelvic bones are both made from metal. These implants have been found to be much more likely to fail, and even the wear caused by normal usage releases metal ions into the bloodstream. The ions destroy bone and muscle tissue, and two of the types of ions released have been identified by the World Health Organization as possible carcinogens (Cohen, February 2012).

2.1. Medical Device Regulations

To try to prevent problems like these, governments impose regulations, which are rules issued by a governmental authority that have the force of law (Merriam-Webster). Since Band-Aids and implants clearly do not need to be regulated at the same level, most regulations, including those in the EU and the United States, split up medical devices into multiple categories. A product must meet different levels of restrictions and requirements based on its category, or class, before it can be brought to market. Figure 2.1 shows a general layout of how devices are divided into classes in the EU. Almost all implantable devices fall into the highest-risk category, which involves the most supervision. The problem with the existing EU regulations, which are used for medical devices in Denmark and all other EU member countries, is that the breast and hip implants mentioned met all the regulations, and still had the described safety issues.

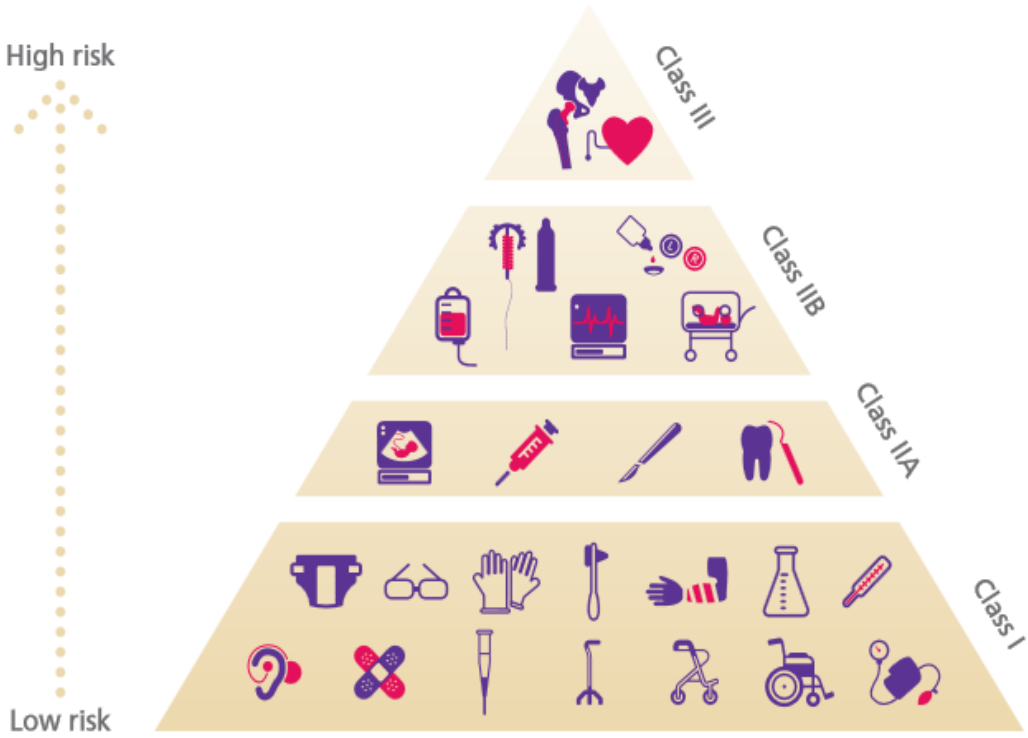

Figure 2.1 The division of medical devices into classes by risk in the EU (MedTech Europe, 2013)

While these examples show the need for more regulation, it is equally important to avoid making the regulations too stringent. The United States has much stricter regulations, and over time, this has resulted in American patients gaining access to potentially lifesaving devices months or even years after European patients. For example, aortic stenosis, a heart disease that obstructs blood flow, is typically treated using open-heart surgery (Aortic stenosis, 2014). Once symptoms appear, patients have a 50% mortality rate over the next two years without surgery, but many of these patients are too frail to undergo surgery. In response, a transcatheter approach, using a new valve inserted through an artery in the leg, was developed. The transcatheter heart valve led to a 20 percentage point decrease in one-year mortality rate for European patients who were unable to get open-heart surgery. The transcatheter technology was approved in Europe in 2007, but as of November 2013, it had yet to be approved for use in the United States due to the slow-moving nature of the FDA approval process, despite being proven effective in European markets (Citron, 2013). Clearly, a balance must be reached between overly lenient and overly stringent regulation.

2.2 The Danish Health Industry

The necessity of writing and implementing new regulations has become increasingly pressing as the health industry worldwide and in Denmark is large and growing. There are currently about 500,000 medical technologies worldwide, comprising 20,000 generic groups (e.g. pacemakers or syringes). The number of devices is rapidly growing, as improved versions of medical devices are developed and introduced approximately every 18 – 24 months. The European market for these devices is already around €100 billion, or 10.4% of the EU's combined GDP (MedTech Europe, 2013). It is growing 4% every year, compared to just 1.2% for the economy overall (The Economist, 2014). Figure 2.2 (below) provides a visual representation of the statistics from this section.

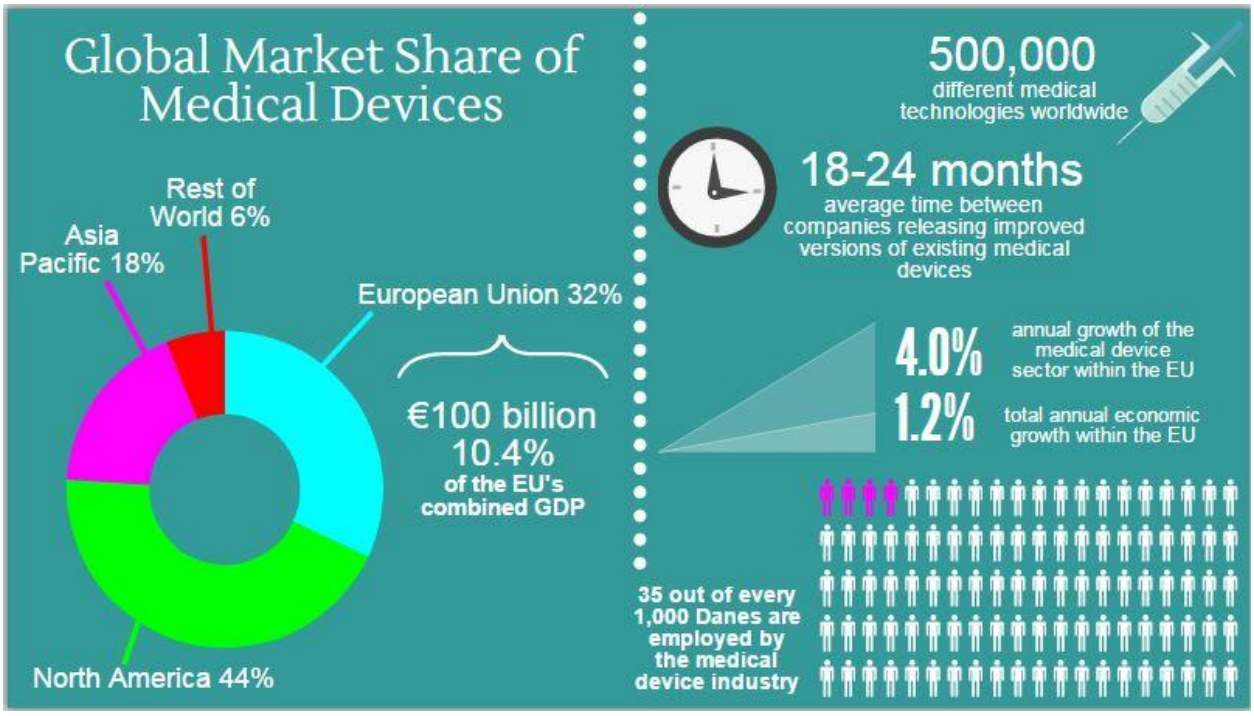

Figure 2.2 Infographic on global medical device statistics (by Sam Jacobs, 2015)

Denmark specifically produces enough medical devices to export €2.5 billion worth every year, and it imports another €1.5 billion. Additionally, 35 of every 10,000 Danes are employed in the Danish medical device industry, the third highest proportion out of the EU countries (MedTech Europe, 2013). The health care industry overall employs 1.7% of the population, and accounts for 12% of exports. While the Danish government clearly has a

responsibility to protect their citizens, they also want to preserve their country's strong international position in the health care industry. In 2013, the government reported their vision for the health care industry:

> Denmark should be among the most attractive countries in the world for developing, testing and manufacturing health and care solutions based on strong research, fast implementation of innovative new technology, good conditions for public-private collaboration and a well-functioning, development-oriented home market (The Danish Government, 2013).

This vision requires a compromise between industry desires for more lenient laws, and patients' need for stricter ones.

The patients are not without representation here; rather, they have several consumer groups working on their behalf. In Denmark, the main consumer group is Forbrugerrådet, the Danish Consumer Council (FBR), which is a member of the larger Bureau Européen des Unions de Consommateurs (BEUC), or European Bureau of Consumer Unions. FBR is a nongovernmental organization that aims to fight for what it perceives as eight basic consumer rights, the first of which is the "right to health and safety" (Forbrugerrådet Tænk, 2011). A major factor in achieving this goal is ensuring that all medical devices are safe for the patients on whom they are used. Therefore, FBR has become quite involved in the debate over what changes, if any, should be made to the current EU legislation and regulations.

2.3 The Process

The EU is currently in the process of writing revisions to their medical device directives, major forms of law that create a legal framework for Denmark, and the EU's other member countries, to implement. In this way the EU determines what must be done (throughout all of the European Union), and Denmark determines how to accomplish that within Danish borders (P. Stapleton, PhD, personal communication, February 16, 2015). To figure out what changes may need to be made, the current policies that govern medical devices in Denmark, and in the EU, must first be understood. How does a medical device develop from the design phase to widespread use in patients around the world? To answer this question, we will illustrate the process with a particular type of device, namely the recently controversial metal-on-metal hip implants manufactured by the company DePuy.

2.3.1 Design Phase

Every medical device starts with a concept. That concept may be original, or, more often, it may be an improvement on an already existing device. The design phase starts when the concept begins to take shape, when goals for the device are defined and a systematic plan is laid out (Alexander & Clarkson, 2000). In the US, during the design phase there is already regulation that needs to be followed (DeMarco, 2011, p. 53), however in the European Union there are only guidelines (Alexander & Clarkson, 2000).

Metal-on-metal hip implants were already in use before DePuy was certified to put their version of the device on the market in 2003. For example, in 1997, the Birmingham Hip Resurfacing (BHR) hip implant was already on the European market. DePuy's motivation for its metal-on-metal hip design, the articular surface replacement (ASR), was competition. A rival company, Smith and Nephew, had taken over the production of the BHR and DePuy was under pressure to create one of its own (Cohen & Billingsley, 2011). Later on, in 2004, DePuy made changes to the design of its ASR implant when designing the Pinnacle, with the goal of increasing patients' range of motion as compared to their previous range of motion with the old implants (Cohen, February 2012). Because this was supposedly a minor design tweak to an already approved device, its new Pinnacle device was able to pass through the premarket approval process at an accelerated rate.

2.3.2 Premarket Approval

The next step in the process after completion of the design is obtaining premarket approval of the medical device. A company's goal at this stage is to obtain a Conformité Européenne (CE) mark for their device, which allows the device to be marketed in any EU member state. The CE mark (displayed in Figure 2.3 below) is actually used for many types of products, but in the context of medical devices it is meant to reflect that "the device successfully performs as intended in a manner in which benefits outweigh expected risks" (Kramer, Xu, & Kesselheim, March 2012, p. 849).

Figure 2.3 The Conformité Européenne (CE) Mark issued by notified bodies

Each country in the European Union has its own government body, called a competent authority, which oversees device approval. Denmark's competent authority is Sundhedsstyrelsen (European Commission). However, CE marks are awarded by notified bodies, particularly when the medical devices are complex. Notified bodies are independent companies designated by a competent authority to approve certain types of devices. They are for-profit and funded by review fees from manufacturers (Kramer, Xu, & Kesselheim, March 2012). Because of this, some have argued that there is an inherent risk of collusion between notified bodies and manufacturers (Cohen, February 2012). As the notified bodies get their profits from companies, they may be motivated to deal with regulations more leniently in order to attract more companies and compete with one another.

The comparison between EU and United States medical device policy is very interesting as the differences are apparent. In the US, all medical devices are regulated by one central authority, the US Food and Drug Administration (FDA). The FDA requires that devices function properly and be effective for their intended use, as well as safe for patients. High-risk devices require clinical studies ensuring efficacy and safety (Kramer, Xu, & Kesselheim, March 2012). The FDA is funded by the US government and user fees. User fees, however, make up less than 20% of overall FDA funding, and there is no incentive for competition as the FDA is the only regulatory authority (Kramer, Xu, & Kesselheim, March 2012). The FDA is a federal agency with a priority on device efficacy and safety in its regulations, while the EU is primarily a trade organization. Therefore it has been argued that the EU is more concerned with promoting commerce than ensuring safety or effectiveness (Kramer, Xu, & Kesselheim, March 2012).

Manufacturers must prove to notified bodies that their devices meet the essential requirements to be approved for market. Essential requirements, according to The 'Blue Guide' on the implementation of EU product rules, "define the results to be attained, or the hazards to be dealt with, but do not specify the technical solutions for doing so" (European Commission, 2014). Medical devices must meet the essential requirements to prove that they are safe for users and patients. An effective way to prove that a product meets the essential requirements is for the company to comply with the EU's harmonized standards. These standards are "technical specifications" recognized by the International Organization for Standardization (ISO) for the manufacturer to continually use. Not all standards must be met for a device to be approved, but if the medical device manufacturer can prove that they abide by harmonized standards (recognized by the European Commission), they can prove to the notified body that they meet the essential requirements, which makes approval easier.

To get approval for both its ASR and Pinnacle hip implants, DePuy worked with BSI, a British notified body. DePuy obtained a CE mark for the ASR in 2003 (Cohen & Billingsley, 2011), allowing the device to be marketed and sold throughout all of Europe. In 2010 the Pinnacle was approved quickly and subject to less testing due to the similarity to previous designs (Cohen, February 2012). In the US, it passed through the FDA 510(k) approval process, which is a shortened approval method intended for devices which are equivalent to those that have already been approved.

The original BHR hip implants were approved in a way similar to that of DePuy's ASR approval. Concerns were raised about patients possibly experiencing internal exposure to chromium and cobalt (potential carcinogens) after a study in 1994 found that metal-on-metal hip implants released these ions. But a mechanical study proved that the implants mechanically functioned properly; therefore, in 1997 the BHR went to European market (Cohen, February 2012). The emphasis here was on proper device functionality, through mechanical testing, not on device efficacy or safety.

In contrast, the FDA did not approve the BHR until 2006 due to safety concerns and the ASR was never approved to go to market (Della Valle et al., 2009). After the FDA requested post market clinical data on the BHR, the safety of the device was called into question. The FDA forced Smith and Nephew to recall the BHR in 2012, at which point the company also pulled it from the European market.

2.3.3 Marketing and Patient Knowledge

Upon obtaining the CE mark, a manufacturer is permitted to promote its medical device throughout the EU member states. How the marketing is done varies from country to country. In Denmark, doctors choose the products that are put in patients, and hospitals are in charge of purchasing these products. In the absence of lists of specific recommendations, hospitals are likely to choose the cheapest option. It is in a company's best interest to make its medical devices affordable, if the company wants to reach the Danish market. However, when medical device manufacturers increase the time to market for a product due to testing, they have to increase the price of the product.

Companies can also use their resources to influence surgeons and doctors toward using their products. For example, DePuy was fined nearly £5 million for essentially paying doctors to use their devices (Cohen & Billingsley, 2011). A company's influence can also be more subtle. It may try to form a relationship with doctors or surgeons through offering them positions as consultants or giving them access to special trainings. Companies may also push their devices through other types of lobbying techniques. EU legislation for medical devices is not only problematic before the devices go to market; there are also significant problems after the devices are used by patients.

2.3.4 Post-market

After the device has successfully made it to the market, manufacturers are expected to track their devices that are used in patients, and report any serious adverse effects.

> Member states [of the EU] are required to establish vigilance systems for post-marketing surveillance. Manufacturers are required by law to report any serious incidents involving devices they produce or sell and if they recall a particular type of device for technical or medical reasons. (Kent & Faulkner, 2002, p. 192)

These reports go into a database that only the governmental agencies are able to access (Kramer, Xu, & Kesselheim, March 2012). Much of this information can be difficult to track down. Often the notified body involved wants to protect the company and will refuse to give information. Confidentiality concerns override disclosure (Thomson et al., 2011).

After DePuy's ASR implants went on the market, concerns were raised about the toxicity of the metal involved. Also, when the Pinnacle implants went on the market, there were concerns

about basic flaws in the new design potentially leading to higher joint failure, among other things. The British notified body, BSI, that had approved both the Pinnacle and the ASR, did not comment on whether it was aware of these issues during the approval process, saying it was bound by strict confidentiality to DePuy (Cohen, February 2012).

If the adverse effects are too severe or too common, this can lead to device recalls, lawsuits, or stricter regulation governing that device, depending on the situation. In the case of the ASR, DePuy recalled the devices in August 2010, and faced many lawsuits (Cohen, February 2012). In the case of the Pinnacle, the consequences in the EU differed from those in the US. In the EU there are no directives which call for an investigation into similar products from different manufacturers when there is a recall. The recall of the hip implant from DePuy did not trigger a wider investigation into the safety of hip implants from other manufacturers.

In the EU, after the design flaws became known, the British competent authority (the MHRA) convened a panel composed of eight members to try to understand the risks involved. Three of the members had conflicts of interest; two were DePuy consultants and one was the director of product development at Smith and Nephew (Cohen, February 2012). They advised that patients sign a consent form which told them the risks involved before getting one of the hip implants. This advice was not publicized widely, however, and many surgeons and patients were left in the dark (Cohen, February 2012). The complex EU medical device regulatory system is displayed in Figure 2.4.

In the US, the FDA had stricter consequences. First, the FDA moved hip implants to the high-risk category. High-risk devices cannot go through 510(k) approval (see Section 2.3.2 Premarket Approval). Next, the FDA required post-market studies from 20 manufacturers. The FDA also contraindicated use in women of childbearing age (Cohen, February 2012).

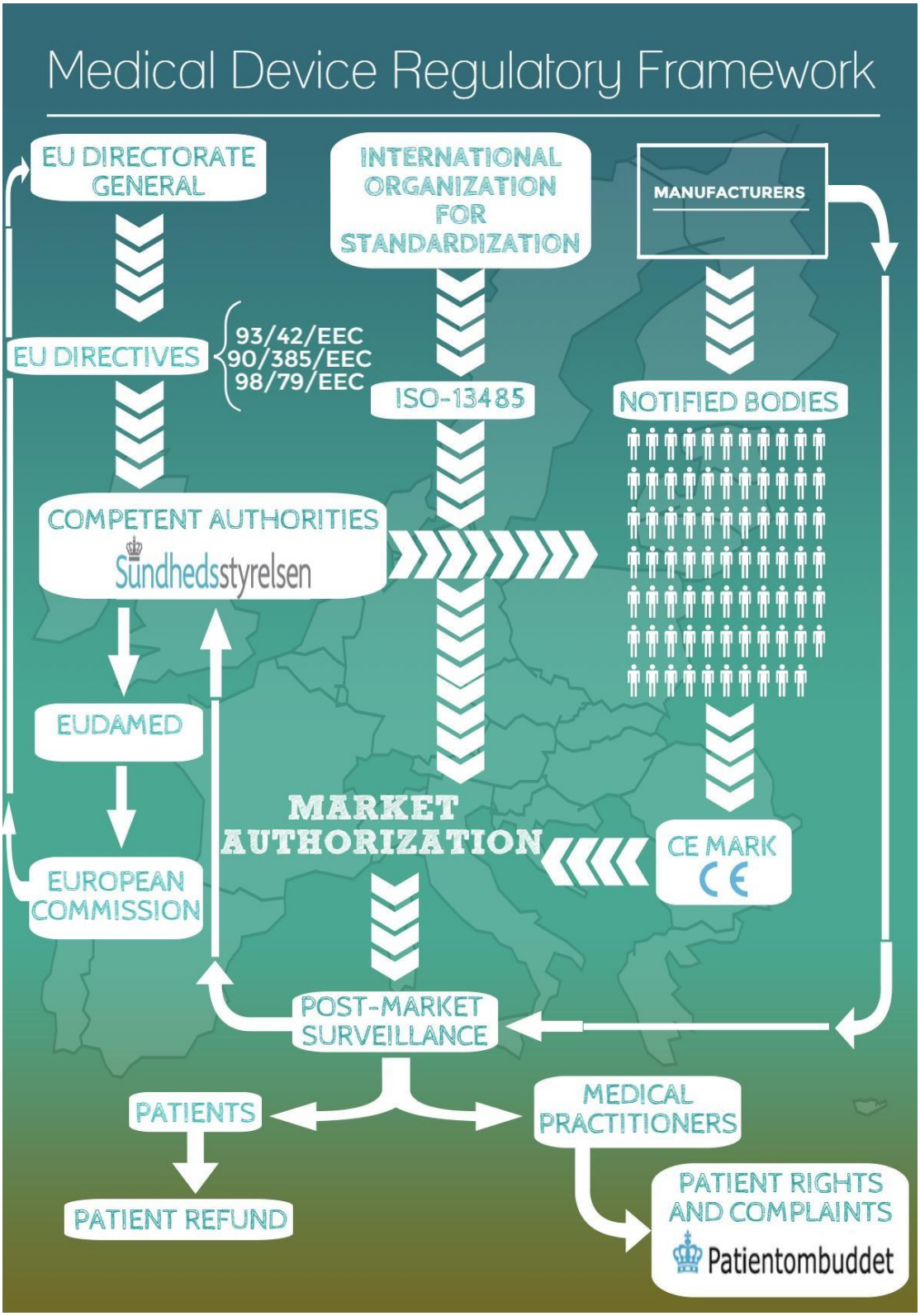

Figure 2.4 The Medical Device Regulatory Framework (Sam Jacobs, 2015)

Metal-on-metal hip implants and other flawed devices, like PIP breast implants, have raised concerns among many about patient safety under the current regulatory system. Failure to protect patients before and after the medical devices go to market has resulted in many organizations, such as FBR and the BEUC, calling for change. Talk of revision is underway, and there are two main alternatives for reform that have been proposed. One approach introduces a centralized overseeing body that would manage approval of the highest-risk devices. This approach was met with strong opposition from the industry and the member state authorities (Altenstetter, 2013). Clearly, any revision is only feasible if it can satisfy needs of all stakeholders involved.

2.4 Industry and Consumer Positions

Before any legislative changes can be made regarding medical device regulation, understanding the groups on either side of the issue is essential. The medical device industry and consumer groups have different motivations, which push them to use different tactics to achieve their goals regarding the change of medical device regulation.

2.4.1 Industry Goals

The medical device industry, domestic and foreign manufacturers, corporations, and industry associations like Medicoindustrien, would like to see medical devices in the EU further deregulated, or held to the same standards as they are currently. While deregulation typically comes at the expense of patient safety and ethics, it is critical to remember that any industry, including the medical device industry, is first and foremost a profit-driven enterprise. Increased regulation cuts into profits as companies need to pay notified bodies, fund research and development, test their devices, and delay full-scale production and sale of the device until the regulatory process has been completed and the product has been certified. Furthermore, the manufacturers cannot be expected to act in the best interest of the consumer (or patient) before business interests, beyond what is mandated by current legislation. In 2002, the Journal of International Business Studies conducted a survey which shows how low responsibility to society and respect toward ethical norms rank relative to growth of business and personal wealth in a business person's mind (Figure 2.5). The study surveyed 1,814 business students and professionals in 21 countries across the globe and used their answers to effectively rank the 15

business goals targeted within the survey. If a sample of 1,814 individuals from around the world is any indication, the business professionals working as manufacturers and retailers of medical devices in the EU will not sacrifice business growth and continuity of business (priorities 1 and 2, respectively), for the safety of consumers (priority 8) (Hofstede et al., 2002).

TABLE 2
MEAN RATED IMPORTANCE OF 15 BUSINESS GOALS ACROSS 21 COUNTRY/ UNIVERSITY GROUPS

(standardized data; rank 1 = most important)

	For Tycoon		For Self	
	Rank	Score	Rank	Score
growth of the business	1	1.26	1	1.00
continuity of the business	2	1.05	2	.86
this year's profits	3	1.01	9	.26
personal wealth	4	.83	10	.08
power	5	.68	12	−.62
honor, face, reputation	6	.47	7	.48
creating something new	7	.21	6	.49
profits 10 years from now	8	.15	5	.56
staying within the law	9	−.12	4	.59
responsibility towards employees	10	−.30	3	.64
respecting ethical norms	11	−.52	8	.30
responsibility towards society	12	−.82	11	−.06
game and gambling spirit	13	−1.09	14	−1.57
patriotism, national pride	14	−1.26	13	−1.28
family interests	15	−1.56	15	−1.73

Figure 2.5 Survey results from a 1,814-person study ranking business goals (Hofstede, 2002)

2.4.2 Consumer Group Goals

Consumer groups, including FBR, are spearheading the campaign to push policies and legislation forward which will make medical devices safer for consumers. There are many consumer groups around the globe that push for consumer rights. Forbrugerrådet is a powerful non-governmental organization based in Copenhagen whose mission is to prioritize consumer health, safety, and rights in Danish markets. Forbrugerrådet specifically works to advocate for the rights of all consumers while actively remaining unbiased from any public or private persuasion (Statutes of the Danish Consumer Council, 2015).

2.4.3 Industry Resources

Medical device companies with many resources (money, lawyers, information) are able to use access goods to gain access to an EU institution or position, through which they are able to influence policy making. These access goods are, as defined by Pieter Bouwen, pieces of information "provided by private actors to the EU institutions in order to gain access [to EU Institutions]. Each access good concerns a specific kind of information that is important in the EU decision-making process" (Bouwen, 2002). These goods allow them to wield their influence within said institution to influence policy-making. Despite the fact that many of the medical device companies are medium to small sized, they are in a highly profitable field, and can therefore afford these access goods. Thus, medical device companies can be very influential in EU regulatory decisions.

2.4.4 Consumer Group Resources

Forbrugerrådet employs many resources to push policy and legislation changes through Danish and European legislative bodies. Similarly to companies in the medical device industry, FBR uses lobbying to push agendas on consumer rights through by providing multiple types of access goods, including 'expert knowledge' (EK) (Bouwen, 2002). *Forbrugerrådet Tænk* and *Forbrugerrådet Tænk Penge* are two regular publications published by FBR; through these publications, the consumers and employees of FBR become more educated on the current state of consumer goods. The information, technical or otherwise, garnered by consumer groups can be considered as EK and helps FBR have a voice in the policy making process in Danish and EU institutions. Change in policies and standards regarding consumer rights do not only unfold through lobbying; FBR in particular employs other methods to incite change.

FBR, a non-governmental organization, does not have the same amount of financial resources available as medical device companies, so it has to turn to means other than lobbying frequently. Publications, debate, and awareness-raising are common methods of educating consumers for consumer groups (Forbrugerrådet Tænk 2011). FBR has had great success with launching social campaigns to raise awareness, inform the consumer, and bring industry changes. In 2009, FBR worked to launch a campaign to prevent endocrine disruptors (EDCs) from being used in consumer goods. There had been increasing evidence which suggested that EDCs were causing serious problems in the development of children but no hard evidence had been proven,

so EDCs were continually being included in many common household consumer goods such as antiperspirants and some shampoos (Sørensen, 2011). Without the real ability to change legislation, FBR launched a campaign to educate consumers on how prevalent EDCs were in lotions, sunscreens, and other common goods. They employed a method where they asked companies to cease producing products with the harmful chemicals; if they refused, FBR put them on a 'shame' list which was given to consumers while they shopped. The use of press coverage and the campaign empowered the consumer to be informed and it resulted in 24 companies stopping the use of EDCs. The case of this campaign proves the efficacy of enacting change to better the common good while avoiding lobbying to change legislation. By utilizing other methods, consumer groups may have a better chance to induce change to protect consumers than by using lobbying methods for legislative change.

2.4.5 Industry Motivation

Breakthrough medical device approvals are near an all-time low according to the FDA. Some believe that excessive regulation makes it impractical for companies to spend money toward breakthrough ideas. These regulations have added to the time and cost required to bring a new, innovative, medical device to market. There is only a small market for most medical devices, meaning the manufacturer faces smaller profit margins for each new line they produce. At some point, such small profit margins are not worth the company's effort, and the company learns to stop pursuing new devices. Additionally, most medical device companies are either mid-sized or small companies. Smaller companies often tend to lack the capital to invest lots of money up front for a long-term return (Kirisits & Redekop, 2013). By tightening industrial regulations, the regulatory bodies have cut down on profits drastically enough to begin strangling the industry through starving companies of their motivation. This financial burden is even enough to deter many start-ups and new technologies from finding their place in the medical device industry, as it ups the amount of money required to make headway with a high-risk device.

In attempting to save patients from potentially dangerous medical devices, FDA regulations are preventing terminally ill patients from undergoing high-risk procedures that could possibly save their lives. Paul Citron, a founding member of the American Institute for Medical and Biological Engineering, believes that "the paradox is that the FDA's current regulatory

approach may be causing unnecessary patient suffering and death by virtue of the regulatory delay imposed by its requirement" (Citron, 2013, para. 11). This is the area where most of the ethical debate surrounding medical device regulations arises. A deep-brain stimulation method to reduce Parkinson's symptoms, a left ventricular assist valve, and a cutting edge pacemaker, among many other devices, were granted a CE mark from the EU and saved, or dramatically improved, the lives of patients many months before the company was granted FDA approval. In the case of an already safe device, waiting on FDA approval only limits the amount of time that ill patients have to undergo necessary procedures.

2.4.6 Consumer Group Motivation

Forbrugerrådet, along with other groups, has found evidence that the medical device industry needs more regulation in place because even the most basic of consumer rights are being violated by the current system. In 2012, FBR and BEUC released a publication which states that the current medical device regulation does not comply with the basic consumer right to have access to safe consumer products. According to these consumer groups, it is unethical that medical devices, especially high risk ones, do not "undergo [a] thorough assessment" to ensure the safety of the device before being put on the market (BEUC, 2012). The publication is not the first to come out expressing concern about the lack of hard evidence ensuring the safety and efficacy which is needed before the medical device goes on the European market. In 2011, *The BMJ* (previously the British Medical Journal) penned an article outlining specific concerns that medical devices on the European market do not necessarily have evidence of efficacy or safety (Cohen & Billingsley, 2011). The authors questioned the ethics of the current legislation, saying that consumers are unknowingly being placed at high risk from devices on the market. Many publications offer evidence and points which are consistent with the arguments put forth by consumer groups that the current legislation on medical devices endangers consumers.

2.5 Our Project

Forbrugerrådet proposed a project involving researching the current EU medical device legislation and from that information, making recommendations for legislative and practical change. Forbrugerrådet asked us to help it provide a solid backing for its proposal, come up with new and innovative reform measures, and ultimately change the EU medical device regulatory

environment. The change would promote consumer safety to the point where Danish patients can be confident in receiving minimal risk medical care. In proposing these reforms, it is necessary to walk the line between the bureaucratic, burdensome approach of over regulation, and the 'wild-west' of dangerously under-regulated medical devices that currently dominates the EU. This requires a comprehensive understanding of both sides regarding medical device regulation issues. In this project, we conducted interviews and surveys to delve into the regulatory environment and provide perspective and details into what a product goes through before ever coming into contact with a patient. The next chapter details our methods for accomplishing our goal.

Chapter 3: Methodology

The goal of this project was to develop recommendations for changes to European Union (EU) medical device regulation that will improve patient safety without stifling innovation. We worked with Forbrugerrådet (FBR) to identify changes that needed to be made to the current regulatory system. To accomplish our goal, we divided our project into the following objectives, (also displayed in Figure 3.1):

1. Gauge the public's confidence in medical devices as well as their awareness of patient rights and the possible consequences of medical devices.
2. Gauge the relative safety of the European Union regulatory environment versus the United States environment.
3. Identify areas where the EU regulatory system could be improved.
4. Determine specific improvements that could be made to the current EU regulatory system.

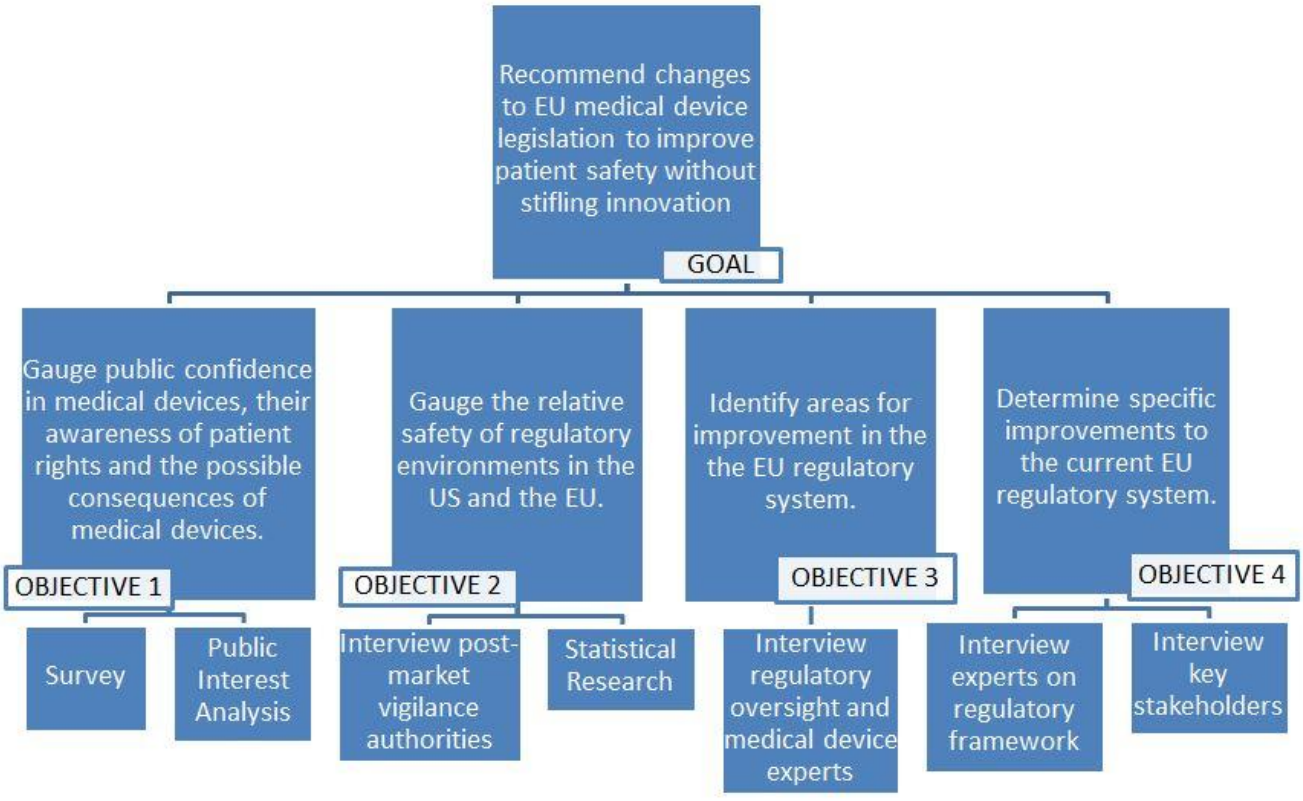

Figure 3.1. Goals, objectives, and methods of our project (Sam Jacobs, 2015)

3.1 Objective 1: Gauge the Public's Confidence and Awareness

Objective 1 stands to identify the channels through which Danes see medical devices and to determine if they would be receptive to changes in medical device regulation. Learning the best way to inform the Danish public and to gain public support for the issue is essential in proposing legislative changes, because change will not occur without a strong public backing. The method we used to accomplish was a public survey in Denmark.

3.1.1 Survey

We included questions for our project as part of Forbrugerrådet's larger online survey. A survey is a highly effective way to obtain and quantify information from a large group of people (Berg & Lune, 2014), which is necessary to determine how much the average Dane knows about medical devices and the related regulations. Some of the questions used a rating scale, in which respondents indicated their opinion on the question using a choice between a maximum and minimum. For example, one question, "How much do you trust your doctor/hospital to choose the right medical device for you," provided the respondents with options ranging from "In very low degree" to "To a great extent." Other questions were multiple choice. The full set of questions used for this survey can be found in Appendix A.

Once all the data was collected, it was analyzed using quantitative methods. The rating scale and multiple choice questions were most easily analyzed quantitatively, such as by finding the average rating or most common response.

The main obstacle here was making sure that our sample size was large enough to obtain sufficient data, and that our sample was as representative as possible of the Danish population. The sample size was not a problem after all; we received over a thousand responses with this method, similar in number to the responses received by a previous Worcester Polytechnic Institute (WPI) student project (Samuel et al., 2014). The sample was not demographically representative initially: about 60% of the respondents were women, and about 43% were over 60 years of age. The survey was also only distributed to FBR's online panel, which means the respondents were a self-selected and most likely socially conscious group. The results were weighted by the FBR survey team to partially adjust for the demographic issues; however the results are still not completely representative of the population due to the self-selecting nature of the process.

3.1.2 Patient Focus Group

With the results from our survey we received 96 email addresses from respondents interested in being interviewed further about their experiences with medical devices. We planned to cross-reference their responses with their region and whether or not they had an implant in order to obtain a representative sample to reach out to and ask if they would participate in a focus group. A focus group is a small group of people brought together to have a discussion and answer questions about a topic of interest. It provides a way to gain a more personal perspective on an important issue, such as medical device safety, as well as allowing the participants to interact with one another and share ideas.

Due to minimal interest and scheduling issues, in the end we were not able to conduct a focus group. While we were unable to gain qualitative data from a focus group, our efforts culminated in two relevant interviews. One respondent with an implant was willing to talk to us over the phone about her experiences as a patient and the information presented to her by her doctor. To protect her privacy, we will keep her name anonymous. Another respondent, Finn Andersen, a representative from Underwriters Laboratories (UL), was able to give us his perspective on regulatory issues through a phone interview. UL is a nonprofit company that performs tests for medical devices and many other products. It is one of the leading certification bodies in the world with a notified body in the UK. To see the list of interview questions, see Appendix B.

3.1.3 Public Interest Analysis

We performed public interest analysis to quantify Danish interest in and knowledge about issues regarding medical devices. This research involved an interview with Morten Dahl Nielsen who works at Sundhedsstyrelsen (the Danish competent authority) with Danish legislation on the advertisement of medical devices. From our interview with him, we learned more about how patients and doctors are exposed to medical device advertising. Our specific findings from this interview can be found in chapter 4. In addition, we looked at articles about medical device recalls in the European Union to see how prominently and thoroughly they are portrayed in the Danish media.

3.2 Objective 2: Gauge the Relative Safety of the European Union Regulatory Environment vs. the United States Environment

Objective 2 helps to reinforce the need for reform in the EU's medical device regulation policies. Data gathered on the relative safety of the European Union's vs. the United States' regulatory environment provided a quantifiable basis for our project. This was critical to the success of our project because in order to show that reform is necessary, we first needed to determine whether a problem exists. A method we used to better understand the safety of the EU regulatory environment was conducting semi-structured interviews with various post-market vigilance authorities who deal with medical device adverse event data. Additionally, we looked through medical journals, government-provided resources, and independent studies detailing circumstances of medical device failures.

3.2.1 Interviews with Post-Market Vigilance Authorities

We corresponded with three post-market vigilance authorities: Martin Bommersholdt from Patientombuddet (also known as the Danish National Agency for Patient Rights and Complaints) as well as Peter Jakobsen and Birgitte Frost from Patienterstatningen (also known as the Patient Compensation Association). These professionals work with adverse event data, which consist of information about occurrences that were or could have been harmful to patients.

To obtain interviews with these individuals, we contacted them with a Forbrugerrådet email address. This gave our group greater credibility, providing concrete evidence that we were working directly with Forbrugerrådet on these issues. Our FBR liaison, Sine Jensen (Senior Health Advisor), was also able to help us get in contact with the relevant experts through her influence and professional contacts. In our emails, we specified that we were US students and we included an abstract of our project in each email we sent out. This helped to ensure appropriate expectations for the interviewees for each interview.

Because our interviewees were well-informed individuals, we used semi-structured interviews. This format allowed interviewees to introduce new ideas, issues, or complications we had not previously considered, while still making sure that our questions were addressed. Additionally, the semi-structured interviews contained open ended questions, designed to allow our interviewees to provide detailed qualitative responses that we could quote in support of our findings.

Our interview questions are further detailed in Appendix B, and these interviews were meant to not only answer our questions on the relative safety of medical device regulatory systems, but also to tie into our upcoming objectives. The interviews overlapped between different objectives, which allowed experts to specify issues in the EU's regulatory system that need reform, and even propose to us any reforms they are backing.

3.2.2 Statistical Study

We performed a statistical study to objectively and comprehensively compare the safety of the two different regulatory environments. Our goal was to find failure and complication rates in procedures involving medical devices, as well as the severity of such failures and their effects on patients, in both the US and the European Union. To do this, we searched medical journals, government publications, and case studies detailing medical device failure. We also sought the help of a reference librarian at Det Kongelige Bibliotek (The Royal Library), and she provided us with several additional websites and resources for statistics. Our statistical findings are given in chapter 4.

3.3 Objective 3: Identify Areas for Improvement in the EU Regulatory System

Objective 3 is motivated by safety considerations of the current system explored in objective 2, and necessary for objective 4. To make effective recommendations for regulatory change, both in the European Union (particularly regarding device approval) and in Denmark (regarding post-market surveillance), it was vital that we examine in detail the regulatory system itself to find potential weaknesses. Without this detailed look, our recommendations would be uninformed, at best ineffective and at worst counter-productive. Our strategy for accomplishing this involved receiving information and opinions from experts with varying perspectives and backgrounds. This allowed us to account for any potential biases, and piece together the perceived flaws in the regulations in a more objective way.

3.3.1 Interviews with Medical Device Experts

We broke the regulatory system up into stages to guide our inquiry; the stages of the process outlined in section 2.2 of the background chapter above formed a basis for this. One set

of interviews was conducted with experts on devices, namely doctors and industry representatives, to allow us to better understand the pre-market approval stage of the process. Our sponsor was able to get us into contact with professor and practicing doctor Gunnar Lose, who has investigated many problems with transvaginal meshes used to treat pelvic organ prolapse.

Also, we were able to contact many industry representatives with the help of our sponsor, Sine Jensen. From individual medical device manufacturers we were able to talk to Arne Mølgaard, senior director of research and development at Cook Medical and Peter Bøge, who works in standards at Novo Nordisk. We were also able to talk to Lene Laursen from Medicoindustrien, an organization that represents Danish medical device companies and Danish subsidiaries of foreign companies. Finally, we were able to talk to Morten Dahl Nielsen, as mentioned previously in objective 1.

Our interviews were similar in format to the interviews conducted for our general safety understanding in objective 2 – since our goal was qualitative information on what could be improved, we wanted to allow our interviewees the chance to speak freely about their perspectives. Too much structure imposed on an interview may have inhibited our ability to ask additional unplanned questions and pursue topics of interest further. Planned questions for each of our interviews can be found in Appendix B. Which questions were actually used and any additional questions asked were determined based on the progress of the interview.

From our interview with Gunnar Lose, our goal was to understand what he would change in particular about the regulations, and his experiences with medical devices. From our interviews with industry representatives, our goal was to better understand the medical device approval process, post-market surveillance, and any problems with either. From our interview with Morten Dahl Nielsen, our goal was to determine how advertising changes doctors' views and decisions about medical devices.

We recorded the interviews by hand, as in objective 2 above. Our records consisted of a combination of general paraphrasing and quotes we found particularly relevant rather than a word-for-word transcript of the entire interview. We contacted each of our interviewees before finalizing our findings to ensure we had a correct interpretation of their views and to obtain their consent prior to quoting them. We interviewed in groups of two, to allow one person to take notes and the other to conduct the interview. This also balanced the number of interviewers with

the number of interviewee(s), so as not to overwhelm the interviewee(s). In addition, this allowed our group to conduct multiple interviews on the same day.

3.3.2 Interviews with Regulatory Oversight Experts

The remaining interviews for objective 3 were conducted with regulatory oversight experts. We talked to the experts mentioned in objective 2, as well as Kristine Rasmussen, Inger Kühne, and Neel Larsen from Sundhedsstyrelsen (the Danish competent authority). Our goal here was to understand where medical device problems typically arise and where the reporting system for adverse events could be improved, from the point of the view of the agencies involved in following medical devices after they are used in procedures (namely Sundhedsstyrelsen, Danish National Agency for Patient Rights and Complaints, and the Patient Compensation Association). Our interviews were conducted in the same manner as in section 3.3.1.

3.4 Objective 4 Improvements to the EU Regulatory System

Objective 4 brings all the objectives together to address the main goal of identifying regulation changes. By offering improvements to the current system, positive changes can be made to increase consumer safety while maintaining innovation. The main method we used to accomplish this was conducting semi-structured interviews with government employees, doctors, and medical device industry representatives.

3.4.1 Interview with European Parliamentarian

After identifying specific areas for improvement in objective 3, we researched the proposals for regulatory change, mentioned in the introductory chapter, that have been put forward in the European Union to see if there are any suggested regulations which address problems identified in objective 3. To further our understanding, we interviewed Christel Schaldemose, a Danish representative to the European Parliament, who is very involved with medical device legislation. We used this interview to learn the feasibility of different regulation changes. Understanding how legislation regarding medical devices is received in the European Parliament as well as the process required to pass legislation was essential in helping us identify the feasibility of our proposed changes.

Our planned questions for Christel Schaldemose are included in Appendix B. As with our other semi-structured interviews, which questions were actually used and what additional questions were asked depended on the progress and direction of the interview.

3.4.2 Interviews with Other Experts

In order for us to create effective recommendations, we had to interview the aforementioned experts from the medical device industry and government agencies as well Dr. Gunnar Lose. By understanding the different ideas and motivations of the groups involved, we arrived at a set of recommendations that took all these into account. These recommendations are designed to improve consumer safety while maintaining the current state of innovation of medical devices.

While interviewing for objectives 2 and 3 we also asked questions pertaining to objective 4. We combined interviews for these three objectives to best make use of our interviewees' time. The interviews were conducted in the same manner as those prior. Appendix B includes the planned questions which were used for the interviews. The data was analyzed to gain a better understanding of each group's goals and ideas on how to remedy the problems. In the next section, limitations of our methods are identified.

3.5 Limitations

While using the methods above, we encountered some limitations. These include the scope of the project, a lack of available information, and interview- and survey-related problems.

3.5.1 Scope of Project

This project was initially quite large, in terms of both breadth and depth. This is an issue that affects thousands of devices and millions of people. Our sponsor suggested a few ideas to narrow the focus of the project. We focused on Denmark's implementation of the EU directives, with an emphasis on pre-market approval. Even with the narrower focus, we needed to be careful to keep the big picture in mind and not get overwhelmed by the vast amount of information available. We also had to be open to receiving information on other issues from our interviews, so we did not end up focusing entirely on pre-market approval.

3.5.2 Lack of Available Information

We found it very difficult to gather statistics on medical devices in the EU. The US FDA keeps a comprehensive database of device reports, which we could use to find, for example, the number of recalls and serious complications associated with a device. The EU has a similar database, EUDAMED, but it is not publicly accessible, and very few adverse events are actually reported, so we had major problems finding any concrete statistics.

3.5.3 Interview and Survey Limitations

One obstacle we faced was gaining access to the desired interview subjects. Forbrugerrådet was able to put us in contact with many individuals involved in the industry, government, and hospitals. However, some of the people we would have liked to interview never replied to repeated emails and phone calls, so we were unable to obtain their input and opinions. In terms of our actual findings, we also had to be careful to account for bias in our interviews, although many of our interviewees agreed on major changes that they would like to see.

Another limitation we faced was that we needed to conform to FBR's larger survey format. As a result, several of our intended questions had to be changed or removed. For example, our open-response questions were removed entirely.

We would like to acknowledge here that our project has undergone Institutional Review Board (IRB) approval, and all precautions were taken to protect the names and identities of those surveyed.

3.6 Timeline

TASK	WEEK							
	PQP[1]	1	2	3	4	5	6	7
Send out survey and conduct public interest analysis								
Research safety of different regulatory environments								
Perform statistical research								
Interview doctors and hospital administrators								
Interview industry representatives								
Interview legal and regulatory experts								
Develop recommendations								

Table 3.1 Timeline (by Sam Jacobs)

[1] PQP stands for Preparatory Qualifying Project research

Chapter 4: Findings and Recommendations

This chapter presents our findings and recommendations for change based on what we found using the methods described in chapter 3. The findings are organized by themes – the key issues we noticed time and again in our survey, background research, and interviews. The findings are primarily focused on the key problems in the current regulatory system and how best to solve them (objectives 3 and 4). Elements of our research from objectives 1 and 2 also play a role, particularly in our findings about patient knowledge and the availability of information. We have seven findings total; each is presented as an overview of a problematic part of the regulatory system followed by a set of recommended solutions.

Finding #1: There is a lack of transparency in the European medical device industry in device approval and post-market surveillance.

The lack of information being communicated about medical devices limits the ability of authorities, companies, doctors, and patients to ensure that patients are receiving safe devices. The limited information being communicated along with reduced accountability has made the European Union's medical device industry non-transparent.

While we were working on the statistical study for objective 2 to gauge the relative safety of medical devices in the EU and US, we found EUDAMED (EUropean DAtabank on MEdical Devices), the European database for medical devices. Since it is the most comprehensive database for European medical device information, EUDAMED appeared to be a great place to get information for products in the European market. The database is made available to all the national competent authorities and the European Commission. However, as of 2012, only 334 people in the world had access to this repository (European Commission, 2012), which meant we could not get access to the database. After completing extensive research to see if anyone had completed a study which assessed the safety of devices on the European market, we kept coming across dead ends as no researchers have been able to gain access to EUDAMED. Some researchers include Kramer, Xu and Kesselheim (see their 2012 report[2]). The restricted access to clinical data and post market adverse events prevented us from doing a comparable analysis of

[2] "How Does Medical Device Regulation Perform in the United States and the European Union?" July 2012

device safety in the EU. In comparison, the US system has a database including clinical trial information and post market surveillance information which is open to the general public online.

Of the ten interviews we conducted, seven interviewees, including politicians, doctors, and industry representatives, stated that a lack of transparency with the device approval process, information on the products, and the clinical data is problematic. As a doctor who is entrusted to give medical devices to patients, Dr. Gunnar Lose wants to see a more transparent medical device approval system. He told us that doctors are not given information about the approval document for the product (i.e. how it got the CE mark) so they themselves are uninformed and are unable to inform their patients appropriately. Dr. Lose stated that he would see the outcomes of all procedures using the device be more transparent so that doctors would be confident in the information they are giving their patients. When meeting with Kristine Rasmussen, Inger Kühne, and Neel Larsen of the Danish competent authority (Sundhedsstyrelsen), we were informed that Sundhedsstyrelsen uses their own database with relevant information on medical devices because EUDAMED is not transparent enough for them to get information easily. A database which is supposed to allow competent authorities to communicate information openly can't even be easily used by the competent authorities.

Lene Laursen of Medicoindustrien commented that the medical device industry would like to see more transparency in the system and noted that the industry agreed to it in the proposals currently going through parliament. Post-market data about devices on EUDAMED is not made available to the industry, which makes it difficult for companies to get information on their products post-market. Manufacturers of medical devices benefit greatly from getting post market information on their products because they are able to track customer satisfaction, identify areas for device improvement, and take corrective actions to fix device problems. This is one reason the industry is interested in a more transparent system. Another representative from the medical device industry, Arne Mølgaard, agreed that increased transparency will help in creating a more efficient approval system for all competent authorities, notified bodies, and the industry. Increasing transparency can make it easier for manufacturers, notified bodies, and competent authorities to communicate information throughout the approval process which could reduce the bureaucratic hold ups. European Parliament member, Christel Schaldemose, is a large proponent of transparency in the medical device industry. Christel's overarching recommendation to make the medical device industry safer is to make it transparent. As she

stated, “Transparency on all these issues is crucial. It’s a problem, therefore transparency is extremely important. We are working on strengthening the whole system and what we’re doing now is a major step in transparency and increasing the safety of patients” (C. Schaldemose, personal communication, April 10, 2015).

Because there are many indications that a lack of transparency in the system is detrimental to many parties, we have established several recommendations based on our findings to increase transparency. **We recommend that EUDAMED be made accessible to doctors**. This would make it easy for doctors to get the information they need to inform their patients. Lene Laursen mentioned that the industry would like to see increased transparency especially if they also have the ability to use EUDAMED so they can get information on the use of their devices. The European Parliament is concerned with using transparency to strengthen the medical device regulation system to ensure patient safety. Christel Schaldemose wants the general public to also have access to EUDAMED, as they should be able to research devices on their own so they can be properly informed before giving their consent to a medical procedure.

The information which will be made available to doctors, the industry, and patients should include clinical trial information, post-market surveillance, and vigilance information. All proprietary information regarding the company should remain confidential and the published information should only be made available after the medical device has gone on the market.

On top of the information going into EUDAMED, **we also recommend a registry for all devices going through the approval process with access to the registry given to the authorities, notified bodies, and companies.** This would increase transparency by providing information to all relevant parties. The United States FDA has several databases available to the general public, one of which is the Manufacturer and User Facility Device Experience (MAUDE) which is a list of medical device reports from mandatory reporters and voluntary reporters of “suspected device-associated deaths, serious injuries, and malfunctions.” The FDA also publicly provides databases with device specific information, clinical information, and recall information. The communication and the availability of the information have resulted in transparency with the medical device industry in the United States. This system has significantly increased the transparency in the US system; therefore, we recommend opening up similar information to everyone in the European Union.

Transparency is a broad subject and a broad problem but there are steps which can be taken which will promote openness, accountability, and communication about medical devices. The goal of increasing transparency is to make medical devices safer for patients while helping the device industry remain innovative.

Finding #2: Procedural complications are being reported at unacceptably low rates.

A comprehensive and reliable reporting system is crucial to a regulatory framework seeking to maintain patient safety because it enables the discovery of dangerous, ineffective, or otherwise faulty medical devices that have been released to market. Gaining this knowledge gives the relevant authorities, such as Denmark's Sundhedsstyrelsen, the justification to issue a recall or a Field Safety Notification to mitigate the damage done by errant medical devices or procedures. The EU's current reporting system is ineffective, as proven by multiple failed medical devices. Many devices gained a CE mark via the EU's approval system, while their hazards went undiscovered by EU post-market surveillance. These devices included Cardiac Constraint Devices, the CoSTAR drug-eluting stent, a Zephyr lung valve to treat emphysema, and a medical grade sealant for lung incisions. Although they resulted in collapsed lungs, unnecessarily invasive surgeries with high risks of operative death, and other serious complications, the EU reporting system failed to gather enough information to act and recall these devices. Their risks were only realized when manufacturers sought approval for the same devices in the US, and the FDA's premarket approval testing and clinical trials exposed the safety issues. Upon viewing the FDA's reports, European authorities recalled these devices, after their widespread marketing and exposure to thousands of patients (FDA, 2012). The discovery of failures of various devices including those previously mentioned is detailed in Table 4.1 from a 2012 report published by the FDA addressing EU-approved devices that never made it into American markets because they failed to obtain FDA approval.

I.	**PleuraSeal to seal lung incisions** was approved in the EU with minimal testing. Claimed to be superior to stitches in preventing air leaks and subsequent lung collapse, Pleuraseal was withdrawn worldwide after a US study showed that 3 times as many Pleura-Seal patients had air leaks as those with stitches.
II.	**Trilucent breast implants** were approved in the EU without human testing and implanted in more than 8,000 women. After the soybean filler was found to break down into toxic compounds, causing rupture, disfigurement, and potentially cancer and birth defects, the implants were withdrawn.
III.	**Stent grafts to repair aortic aneurysms** made by many manufacturers were approved in the EU with limited testing. When US approval was sought, FDA found that many of the devices approved in the EU presented severe risks to patients, including blood clots, graft failure, and aneurysm rupture.
IV.	**An elbow implant** was approved in the EU after FDA told the manufacturer that it had been inadequately tested and was prone to fracture. Once marketed in the EU, many reports of implant fractures caused the manufacturer to withdraw it
V.	**Cardiac constraint devices to treat heart failure** were approved in the EU based on limited testing. Testing to support US approval showed that the devices were no better than prescription drug therapy, but subjected patients to invasive surgery, a higher risk of operative death, and precluded necessary bypass surgery for some patients.
VI.	**Over 160 injected dermal fillers** containing poorly tested substances have been approved in the EU, causing high rates of disfigurement, nerve damage and severe allergic reactions.
VII.	**The Pendra glucose monitor sensor,** approved in Europe as the first noninvasive blood glucose monitoring system, was withdrawn after later studies showed that the device was inaccurate and failed to warn of dangerous blood sugar levels.
VIII.	**At least 12 PFO Occluders** implanted in the heart to prevent strokes have been approved in the EU. Later studies conducted for US approval showed that that a PFO Occluder marketed in the EU is no more effective no more effective for stroke than blood thinning medications but, unlike blood thinning medications, cause heart perforation and other serious complications.
IX.	**The CoSTAR drug-eluting stent,** approved in the EU with limited testing, was withdrawn from the EU when a study for US approval showed that patients more often need repeat procedures and suffered heart attacks with CoSTAR than another similar available stent.
X.	**The Biofield device, claimed to detect breast cancer** better than mammography was approved in the EU with limited testing. FDA review showed that the company's studies failed to demonstrate that the device did, or even could, work. It was not marketed in the EU.
XI.	**RoboDoc, a robotic device to drill the femur for hip replacement,** was approved in the EU with limited data. Later studies showed that the device caused serious complications, including tendon rupture, nerve injury, and hip implant failure.
XII.	**Zephyr, a valve implanted in the lung to treat emphysema,** was approved in the EU to replace surgery. A later study for US approval showed that Zephyr was no more effective than surgery, but resulted in more deaths and serious complications.

Table 4.1 Examples of dangerous or ineffective devices that were approved in the EU (FDA, 2012)

This evidence shows that the EU medical device regulatory framework is not a self-regulating system. If a dangerous device is approved, its risks may not be realized at all. In the case of eight of the devices mentioned above, only the FDA's approval system exposed these devices' failures even though European patients were exhibiting side effects which went unreported in the system.

Denmark's Reporting System

Reporting is not only an issue at the EU level, but also at the national level. Denmark's current medical complication reporting infrastructure is complicated and decentralized. It includes three main databases[3] for complaints, inquiries, and reports from healthcare providers, hospital administrators, medical practitioners, patients, and their families. These reports are never centralized to a single database. There are three national agencies that collect these reports[4], but only one of them, Sundhedsstyrelsen, has the power to issue notifications and recalls on medical devices. To comprehend the Danish reporting system, an understanding of the 2003 Danish Act on Patient Safety is crucial. This act passed parliament in June of 2003, requiring frontline healthcare personnel in hospitals (and, when the act was expanded in 2010, general practitioners) to report "adverse events" that they witness to a national reporting system. Additionally, this act allows patients and their relatives to report adverse events at their discretion. Hospital owners are then obligated to act on these reports. The Danish Act on Patient Safety defines an "adverse event" as…

> an event that occurs in connection with health professional activity, including prehospital activity or in connection with supply of and information about medicines. Adverse events comprise known and unknown events and errors that are not caused by the patient's disease, and which either are harmful or could have been harmful had they not been avoided beforehand or for other reasons that did not occur. (Danish Act on Patient Safety of 2003).

Medical practitioners in Denmark are required by this act to report adverse events surrounding the use, misuse, or failures of medical devices to the manufacturer of a respective device. These reports should detail the failure mode of the device, type of misuse, risks, and consequences, as well as identifying information on the device and the procedure. The

[3] EUDAMED, the Patient Safety Database, and the Patient Compensations Association's Database
[4] National Agency for Patients' Rights and Complaints, Sundhedsstyrelsen, and the Patient Compensation Association

information from these reports allows the company to take corrective action on behalf of their product, or even to announce a recall. These companies are also required to send this data along to the Danish competent authority (Sundhedsstyrelsen). Sundhedsstyrelsen may, at their discretion, submit parts of this data to the European Commission. Communication between the national competent authorities and the European Commission is conducted through EUDAMED. EUDAMED is a secure web-based portal functioning as a repository for information exchanged between the aforementioned organizations. This database is far from comprehensive because competent authorities are not mandated to submit the adverse event reports they receive from manufacturers to EUDAMED. Therefore, the majority of adverse event reports and field safety notifications in EUDAMED are provided by a select few national competent authorities (Sorenson & Drummond, 2014).

Doctors may also send their reports to the National Agency for Patients' Rights and Complaints. This organization acts as an appeals board for the Patient Compensation Association and collects reports from doctors, patients, and their relatives on complaints about the care a patient received, violations of patient rights, or procedural complications. This agency works to analyze these reports, as well as compile the information available to them into the Danish Patient Safety Database (which may also include reports from the Patient Compensation Association), and mount campaigns to effect change in hospital practices, or increase patient awareness of the complaint and refund systems available to them. The Agency for Patients' Rights and Complaints lacks the power to issue field safety notices or recalls, and must cooperate with Sundhedsstyrelsen to actively address incoming reports.

The Patient Compensation Association receives similar reports from patients, regarding any problems from their hospital stay or visit to the general practitioner. This serves as a venue where they can air their grievances with the healthcare system and seek compensation for damage done by doctors, surgeons, medical devices, or medications. The organization is run by a seven-member government-appointed board, but rulings on patient compensation are made by lawyers and consulting doctors who are employed by the Patient Compensation Association. The Association does not perform any analysis on the medical data they receive, largely due to its personal nature. However, the Patient Compensation Association is obligated to forward any information requested by the National Agency for Patients' Rights and Complaints to the Danish

Patient Safety Database. The amount of information submitted to this database is dependent on the needs of the National Agency for Patient Rights and Complaints.

Lack of Reporting in Denmark

The Danish reporting system is so complex that the involved individuals only see their own organization's database and can be unaware of the information presented in other databases. This makes it difficult to request specific information from other databases because correlations and trends in reports may go unnoticed. Due to the distribution of all the information, the low reporting rate, and insufficient interaction between these organizations, none of these databases, not even EUDAMED, can give a comprehensive view of the state of affairs of medical devices in the Denmark.

The 2013 Annual Report for Medical Devices was published by Sundhedsstyrelsen after examining various national databases, and found a total of 4,659 new cases involving medical devices and 1,051 different field safety corrective actions issued by either manufacturers or Sundhedsstyrelsen itself (Sundhedsstyrelsen, 2014). In the same year, all Danish databases (not including EUDAMED) collected reports of only 6,000 medical device incidents. Low reporting rates have plagued the Danish reporting system for years, despite a 2013 campaign by Sundhedsstyrelsen which resulted in a slight and temporary increase in reports submitted by doctors. Martin Bommersholdt, Senior Patient Safety Officer at the National Agency for Patients' Rights and Complaints, acknowledges the shortcomings of the current reporting system, claiming that "its strengths lie in working with and analyzing the data it does receive," rather than in collecting said data. The National Agency for Patients' Rights and Complaints currently only receives 10% of its reports from doctors in hospitals. And even though patients and their families are informed of their rights to report to the Patient Compensation Association and Patients' Rights and Complaints, and Bommersholdt believes the majority of Danish patients understand this system and the chance to receive compensation, only 2% of reports at the National Agency for Patients' Rights and Complaints come from patients and their families (as displayed in Figure 4.1). Part of this low reporting rate stems from the recent (2011) implementation of the current patient reporting process, but patient reporting rates have seen little growth over the last several years. Of the reports submitted by doctors, case handlers, or patients, Bommersholdt estimates that the majority are serious complications that occur at

Danish hospitals, and that these reports account for roughly 20% of aggregate severe complications, "such as patient death or permanent impairment" (M. Bommersholdt, personal communication, 2015).

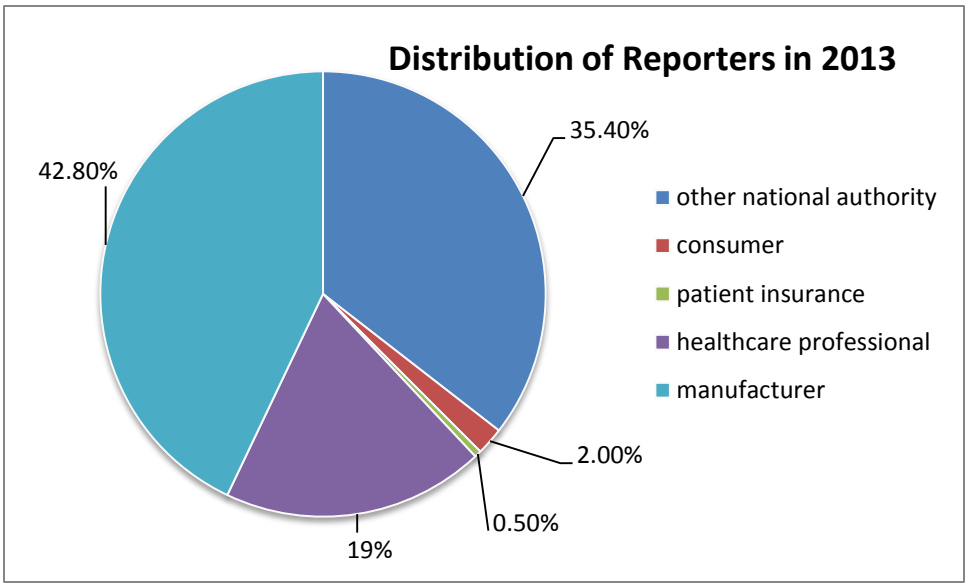

Figure 4.1 The reporting of incident cases by primary reporter (Sundhedsstyrelsen, 2014)

The higher reporting rate for this type of adverse event can be attributed to the high profile nature of such events, which makes it particularly noticeable when doctors fail to report them. Furthermore, Bommersholdt has noticed drastic differences in the availability of information between databases, telling us that Sundhedsstyrelsen "received 1,800 reports of medical devices in a year, and the Danish Patient Safety Database, got in the same period approximately 4,200 events where a contributing factor was medical devices." Clearly different information is being received by different agencies and no one agency can get a comprehensive view. He proceeded to show us the distribution of reports received by his organization, via Figure 4.2, with all categories that made up over 10% of complaints highlighted. This chart shows the low number of reports received for medical devices compared to other reports. We have translated this chart into English.

DPSD Classification: percentage distribution of main classifications of the classified incidents	other regional	hospital	municipality	private
ambulances , emergency vehicles , helicopters , etc .	0.7	0	0	0
Another unintended incident	3.2	5.3	3.6	7.5
treatment and care	1.8	13.6	3.2	7.5
blood and blood products	0	0.9	0	0.4
gases and air	0	0.3	0.1	0.4
referrals in / discharge and medication lists	3.1	9	0.8	1.2
infections	0.2	0.8	1.2	0.2
IT, telephone, infrastructure, buildings, etc...	1.4	2.4	0.1	1
surgical treatment including ECT , anesthetics , etc.	0.3	1.7	0	3.5
medication including liquids	48.2	22.7	66.4	28
medical equipment, aids , x-rays etc..	1	3.5	0.4	4
transmission of information , accountability , documentation	4.3	12.9	1.7	10.1
patient identification	4.2	4.6	0	7.1
prehospital handling	1.6	5.8	21.7	14.4
patient accidents including falls and burns	0.7	0	0	0
samples, surveys, and test results	18.5	12.8	0.1	7.5
self-harm and suicide	0.3	1	0.1	0.1
healthcare visitation, phone consultation	8.8	1.9	0	1.6
technical Allocation	0.7	0	0	0
not completed	1	0.8	0.7	0.6
grand total	100	100	100	100

Figure 4.2 The Distribution of Reports Received by the National Agency for Patients' Rights and Complaints. (M. Bommersholdt, personal communication, March 24, 2015)

Underreporting is an issue affecting organizations other than the National Agency for Patients' Rights and Complaints. When asked if the number of complaints his organization receives accurately reflects the problems that Danish patients encounter, and if patients are aware of the compensation system, Peter Jakobsen, of the Patient Compensation Association, responded "there are a lot of cases we don't hear about. We can see that if they give information in the media about us, then we have many new cases…It's difficult to say how many we don't hear about." Jakobsen also informed us that all doctors in Denmark are required by law to verbally inform their patients of the refund system.

We interviewed one of these doctors, Gunnar Lose, who is both a professor and a practicing gynecologist. He has long been a critic of the reporting system, and published a paper in 2010 on the lack of adverse-event reporting by the medical community. This paper investigated the lack of reporting of complications with transvaginal mesh. Dr. Lose prefaced it

by saying, "it has been known for many years that it [complications] is underreported. There were none [mesh complications reported]. It should be several hundred, possibly thousand." It is widely recognized that Danish medical professionals are failing to report adverse events, despite their legal obligation. Several of our interviewees, including Kristine Rasmussen at Sundhedsstyrelsen, and Dr. Lose agreed that most doctors use similar excuses to justify their non-reporting. The three major excuses are that doctors claim they lack the time to submit reports, are unaware of what needs to be reported, or do not know how to report adverse events. Our research refutes all of these arguments.

Doctors Need to Report

First and most obviously, it is in the best interest of these doctors to make time to file reports, as doing so could take faulty medical devices out of their hands in the future, reducing their liability. Other reports will subsequently increase healthcare provider awareness and patient safety, making their jobs easier. Any basis for the second argument has already been remedied. The legislation provides a very clear, objective definition of the term "adverse event" (provided earlier in this section). Additionally, national health authorities have, according to Dr. Lose, run several campaigns in which they worked with hospital administration to disseminate information on reporting requirements throughout hospitals. And finally, the third argument, that doctors do not know how to report complications, is a fundamentally weak argument. Sundhedsstyrelsen's website links to the reporting form, which is easily located. The form to submit complaints is a very specific (mostly) multiple-choice questionnaire. It works to avoid patient or doctor bias by using this format, and allows for traceability of medical devices and pharmaceuticals back to a specific hospital or medical practitioner. According to Dr. Lose it can be fully completed in less than five minutes. Despite the form's simplicity, Kristine Rasmussen (of Sundhedsstyrelsen) claims that she often receives incomplete reports. Figure 4.3 shows the incident reporting form.

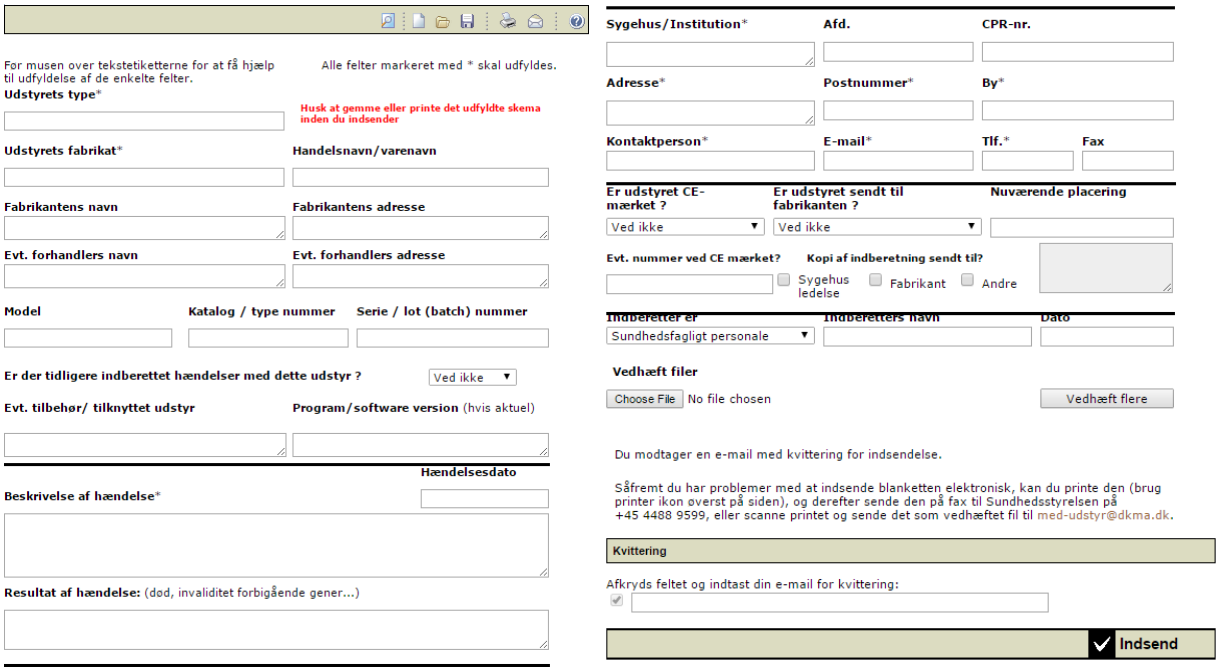

Figure 4.3 Sundhedsstyrelsen's Reporting Form for Incidents with Medical Devices for Healthcare Professionals and Users

Other major reasons for non-reporting are inherent in the healthcare industry. In the words of Dr. Lose, "We [doctors] have a culture where we are not critical to what we do ourselves…we do not like to report side effects." Medical practitioners, attempting to avoid liability for either malpractice or unavoidable procedural complications, often will fail to report these events, as they think it is in their best interest. However, the Danish Act on Patient Safety instituted a system of sanction-free reporting in Denmark, prioritizing learning about medical device complication rates and causes over punishing doctors who make mistakes. While this is intended to encourage doctors to increase reporting rates, these rates have remained low, and Danish authorities have no recourse for doctors who knowingly fail to report adverse events. This is a sharp contrast to how the FDA enforces incident reporting, inflicting criminal penalties for not reporting incidents up to a $1,000 fine and one year imprisonment for the first (unintentional) offense, and as much as a $10,000 fine and 3 years sentencing for subsequent or intentional offenses (Lowe & Scott, 1996). Needless to say, the FDA has a much easier time gathering incident reports from hospitals, having received 937,447 adverse event reports in 2012, compared to Denmark's 7,000 reports in the same year. Due to the regulatory system's lack of

transparency, there is no statistic for the total number of adverse event reports in the EU. However, accounting for the population difference between the Denmark and the United States, America has a population 56.17 times larger than Denmark's, but receives 134 times the adverse event reports. This analysis, in Table 4.2, does not take into account the scale of each country's healthcare system (FAERS Domestic and Foreign Reports by Year, 2014).

	2012 population	2012 adverse event reports
United States	314.10 million	937,447
Denmark	5.592 million	7,000
Ratio (US/DK)	56.169	133.921

Table 4.2 Analysis of adverse event reports received in the United States and in Denmark

All medical device manufacturers are required to implement a notified body-approved post-market vigilance system, and maintain the relevant documentation. This system includes protocols for how the company will deal with the reports they receive, as well as how they will go about issuing recalls or field safety corrective actions. However, post-market vigilance is a reactive approach, and depends on a reliable reporting framework. The onus of post-market surveillance falls upon the notified bodies and the competent authorities. Post-market surveillance is an active approach to improving patient safety. Competent authorities can perform this surveillance by auditing notified bodies, investigating the use of medical devices in hospitals, visiting manufacture sites, acquiring sample devices for testing, and evaluating complaints. Dr. Lose has, in his years practicing medicine, never seen evidence of actual post-market surveillance performed by manufacturers in his hospital. This is indicative that post-market oversight is relying too heavily upon device malfunction reports from doctors, rather than active surveillance by the manufacturers themselves. Even so, post-market surveillance and vigilance systems are meant to work together to protect patient health, and without a robust vigilance system, post-market oversight cannot be at its most effective. This is clearly a problem, since the reports from doctors and manufacturers are not being sent in at acceptable rates.

There are three core issues: doctors' non-reporting, complex and inefficient database structure, and the authorities' lack of recourse against non-reporting individuals. To help

competent authorities and manufacturers notice trends and react more quickly to device failures, complaints, adverse-event reports, and refund requests, a centralized database should exist for all this information. The infrastructure for cooperation between the Patient Compensation Association and the National Agency for Patients' Rights and Complaints has proven effective, so the centralization of all the different bodies involved may not be the most effective solution. There is a need for a centralized database but not a centralized agency. The necessary change is to make clear, transparent communication pathways between these bodies. Information needs to flow freely through a centralized database to be analyzed and interpreted. There are no problems with only Sundhedsstyrelsen (of all the national regulatory authorities) having the power to issue a recall or field safety corrective action, as long as the other organizations can effectively communicate their needs to Sundhedsstyrelsen. In our opinion, the most effective way to increase transparency and communications among these agencies would be to **expand EUDAMED and open it to all**. This way, Danish organizations could concurrently analyze trends from other EU nations, and use this information to preemptively protect Danish patients. EUDAMED currently stores registrations for manufacturers, authorized representatives, and medical devices, as well as certificate data, post-market surveillance data (only provided by competent authorities), and clinical investigation data. EUDAMED could be expanded to include traceability information from hospitals, (anonymized) patient complaints and refund requests, training procedures, the standard of evidence the device was held to by a notified body for device approval to help normalize standards of evidence for similar devices between notified bodies, and the device's approval record. All competent authorities should be mandated to submit this information to EUDAMED. Links to FDA approval-related studies for the same devices could also be included, to catch device failures similar to the devices described earlier in this section in Table 4.1. This would allow for better cooperation between EU member states, the European Commission, and national authorities from different countries, as well as a shorter response time to medical device failures.

To remedy the lack of reporting by healthcare professionals, there are two basic approaches. Danish authorities have been attempting to use positive reinforcement, or at least a lack of negative consequences, to encourage doctors to report complications. By introducing sanction-free reporting, Danish legislation has effectively established a reporting system where there is no downside to doctors filing adverse event reports. However, this positive

reinforcement has not been enough motivation. And since it would be difficult to justify government spending on incentivizing doctors (public employees) to fulfill their job responsibilities and abide by the law (to file these reports), Danish legislators need to drop the metaphorical carrot, and pick up the stick. Emulating the FDA's approach to this problem, **Sundhedsstyrelsen should introduce penalties for doctors who fail to file adverse event reports**. This does not violate the Danish policy of sanction-free reporting, as doctors could only be penalized for failing to report malpractice. It may seem hard to enforce, but if Sundhedsstyrelsen were to run a campaign to increase reporting by patients and their families by promoting awareness, then the competent authority could match patient reports to doctors' reports, and find cases where doctors failed to report. With any luck, Sundhedsstyrelsen would barely have to enforce this, as the fear of such a dire consequence for failing to complete such an easy task would drive doctors to submit these reports consistently. While penalties imposed by the FDA may seem draconian, filing these reports is not a difficult thing to do, and patients' lives are at stake. And despite the fact that the current reporting forms are quick and easy, these forms could be made even more accessible if they were incorporated into the standard post-procedural paperwork, and then sent to the manufacturer by the hospital's case handler.

Finding #3: Patients are unaware of the risks involved with medical devices since information on the safety and efficacy of medical devices is not available to the general public.

A problem related to the lack of transparency and reporting issues discussed above is the lack of information available to patients about medical devices. All European patients have the right to informed consent: "Every individual has the right of access to all information that might enable him or her to actively participate in the decisions regarding his or her health; this information is a prerequisite for any procedure and treatment, including the participation in scientific research," (European Charter of Patient Rights, 2002). A crucial component of informed consent is making information available to the patient. If patients are not properly informed, they do not know enough to make an appropriate decision regarding their treatment. And it seems that patients are not always properly informed. Indeed, in our survey, one of our questions was "Were you informed about the safety of the equipment used? [in your last medical procedure]," and 57% of our respondents chose the option "No, I got no information."

Some of this is due to the transparency issues described in Finding 1, but there are other problems as well. According to Dr. Lose, though there are guidelines on doctors informing patients of the relevant details about medical devices, it is his impression that most doctors forget to give this detailed information. But it is not unreasonable to expect doctors to properly inform their patients. For example, in our interview with a Danish patient (who shall remain anonymous), we found that she was well informed by her doctor about the hip implants she received. According to her: "Yes, I did [feel comfortable with the information given]. I was told how it functions… I feel I get the knowledge I want." All patients throughout the EU should be given sufficient information, as she was.

Even when the appropriate information is made available to patients, however, there is an additional problem which Christel Schaldemose brought up: "We end up maybe with a system where people sign without reading; as we do on the internet: e.g. 'I have read and understood the following.'" To overcome this, **we recommend that the information provided to patients be simplified to the extent that the average layperson can read and understand the information in 15 minutes**. This serves two purposes. First, it motivates patients to read through it all. Second, it allows companies and doctors some discretion in the level of detail presented. For instance, if a device has many potential complications associated with it that have occurred in only 1 of 10,000 people, this might not be necessary to include in the initial information given, particularly if the patient involved does not fit the characteristics associated with those risks.

The content of the information is just as important as the level of detail in which it is presented. Determining precisely what this content should be is a difficult task; indeed, it would be an entire project in itself. According to the BEUC position paper on medical device regulation, "For implants, as part of giving informed consent for surgery, consumers should be provided with a document on the specific product used, its characteristics, the Unique Identification number, the potential risks and also additional information on the post-operative follow up measures associated with the implant," (BEUC, 2012, p. 9). And according to a BEUC position paper on a similar issue, the content of information made available about pharmaceuticals, "Patients need information all along the patient journey, including information to understand if something is wrong, information that gives them a realistic idea of the evolution of their health status, help them to understand when further investigations are preferable, to know what treatments exist and what they can expect from them, and help them share or make

informed choices," (BEUC, 2010, p. 4). Building on this, **we recommend introducing a standard for what information about medical devices is given to patients: for example, information on the testing done on the device and the associated risks and side effects**. A standard for information content would ensure the availability of the right kind of information for motivated patients to better judge their own safety in relation to medical devices.

The variety of people and agencies involved in the case when a problem arises with a medical device could be potentially overwhelming to a patient: his or her doctor, the hospital, the Patient Compensation Association, the National Agency for Patients' Rights and Complaints, the manufacturer, Sundhedsstyrelsen and the list goes on. To resolve this, **we recommend that patients be given better guidance on whom to contact in the case that a problem arises with their device or procedure.** A triage system can be introduced – rather than the doctor determining where a particular issue should go; patients can call a designated phone number and be directed on which agency to contact.

The existing proposals in the European Parliament at this time do not discuss the issue of giving patients access to more information, either from the doctor before a procedure or in online form through a public database. This is partly because some of these issues are governed on a national level, according to Christel Schaldemose. She thinks that the Danish government has tried to make sure that patients are informed. And according to Morten Dahl Nielsen, Denmark has national legislation on advertising of medical devices, including a general requirement that advertising of medical devices must be factual. To bring this success to the EU level**, we recommend that the information provided to patients across the EU be made more consistent**. Patients everywhere should have the same access to information about the safety and efficacy of medical devices. Denmark's system can be used as a model for implementation in other EU member states.

Finding #4: There is currently much debate about whether full clinical trials or reviews of similar devices are appropriate for most devices.

Whether or not clinical trials should be required for all devices before approval revealed itself as our most controversial finding. Currently, clinical trial data is only required for approval if the notified body with whom the manufacturer is working requests it. Otherwise, the clinical data presented to show the device is safe and effective can be anything from a review of

literature on similar devices to a small-scale animal or human trial. Most industry representatives would like to see the current system, or something similar to it, stay in place. Arne Mølgaard from Cook Medical told us that running clinical trials "costs a fortune," so manufacturers prefer to examine safety in other ways whenever possible to prove safety for the patients. Peter Bøge, who works in standards at Novo Nordisk, went even further, claiming that "the whole market would collapse" if clinical trials were mandated. He also argued that, for the most part, they are unproductive: many of the complications that have arisen with medical devices would not have been caught by trials. Lene Laursen at Medicoindustrien believes that the rules for approval should be tightened to some extent, even if that does lead to an increase in the number of clinical trials that must be performed. However, she cautioned that clinical trials are not "suitable" for every new device, and that "it would be a mistake to put all the products in very rough boxes," rather than evaluating the need for trials on a case-by-case basis.

On the other side of the debate are people such as Dr. Gunnar Lose, who argue for a far stricter clinical trial system. Lose himself frequently tells the story of a transvaginal mesh for which the clinical data consisted of a single trial examining the performance of the mesh in eight sheep. Sheep have a rather different anatomy than humans, and the mesh later ended up failing in many patients after implantation. Lose believes that all new products should be subject to at least phase II trials, in which the safety and effectiveness of the device are examined. For comparison, most manufacturers currently use preclinical (before phase I) data, which does not involve using the product in any humans. Trials can go as far as phase IV, which examines long-term risks and benefits, as well as effects in different populations, based on data from hundreds or thousands of patients after the product is placed on the market. The first three phases of clinical trials, which would all occur before a device is placed on the market, are outlined in Figure 4.4. Additionally, though it applies to just a small subset of devices, 96% of the membership of the British Association of Aesthetic Plastic Surgeons (BAAPS) thinks that dermal fillers in the UK should be required to meet the same, more stringent standards they are required to meet in the US.

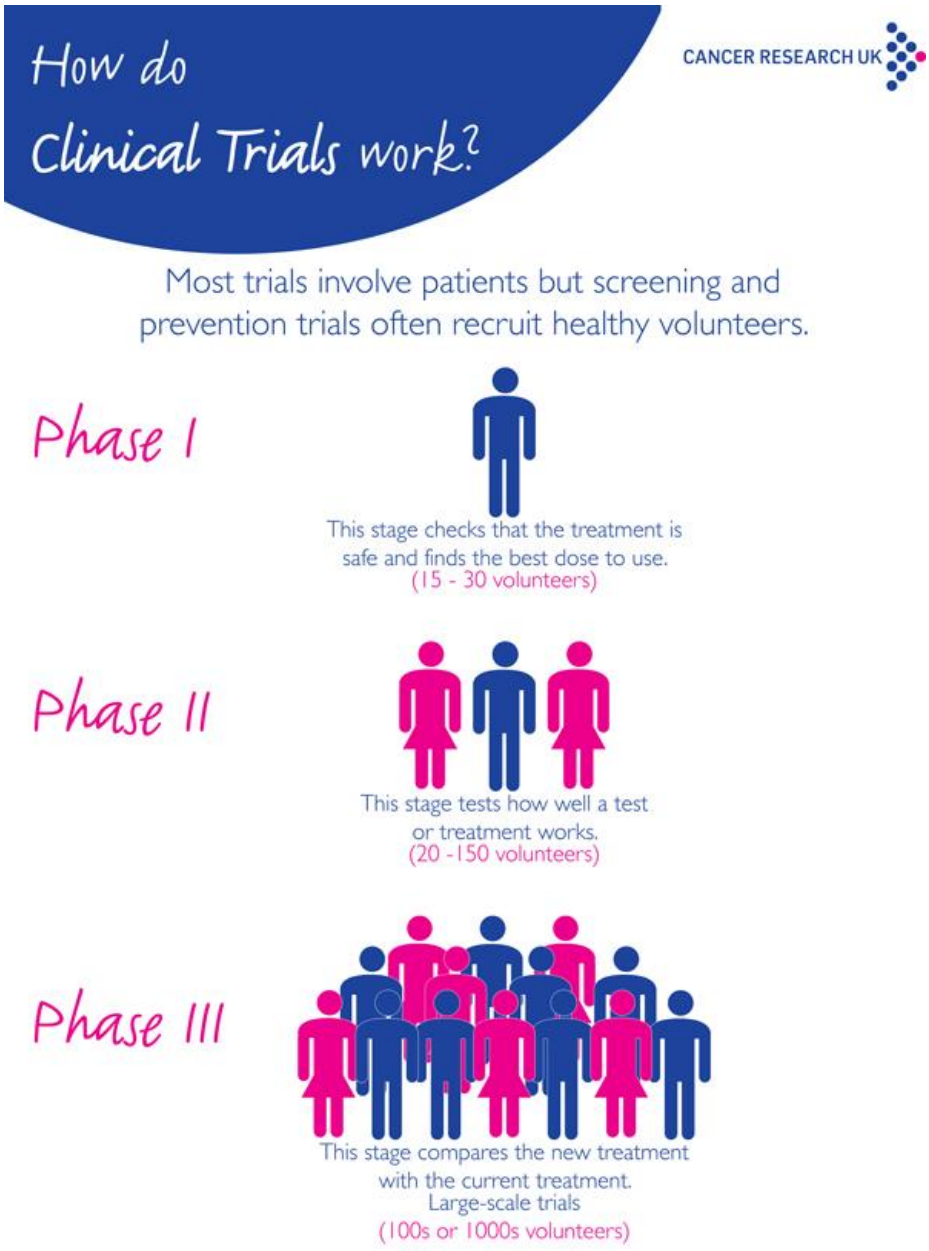

Figure 4.4 Pre-market phases of clinical trials (Arney, 2012)

With these sharp differences in opinion, we needed to go back to data we had collected, particularly relating to comparisons between the US and EU systems. For the 80% of devices considered low to moderate risk, neither system requires clinical trials, and few people would argue that either should. However, unlike the EU system, the US Food and Drug Administration's (FDA) approval process requires full clinical trials for all new high-risk devices. One study, described in Finding 2, discovered 12 different devices that were approved

in the EU before testing in the US found evidence that the devices were either ineffective or unsafe (FDA, 2012). There may even be more similar cases, but due to the lack of available data discussed in Finding 1, it is essentially impossible to perform a comprehensive study. However, there is one important caveat: the devices were approved in the EU well before they would have been approved in the US. In general, devices are approved in the EU two to three years before the US. For the devices in the study, this delay was beneficial because a flaw was found in that time, but for the majority of devices that are safe and effective, it is not. For certain devices, the delay can have an enormous cost in terms of death and lost quality of life for US patients, because they have to wait longer for the devices to be approved before treatment.

Our recommendations had to account for these differing opinions and the benefits and drawbacks of full clinical trials. The cornerstone of our plan is to **regulate clinical trials at the European level, rather than leaving the entire decision up to the notified bodies**. This ensures that all devices will be subject to testing and scrutiny, thereby increasing their safety. **For new high-risk (classes III and IIb) devices, at least a phase II trial, as described above, would be required**. These trials provide a good pre-market indicator of safety without being unduly burdensome. For any device with a very similar predicate device, at least a phase I trial would be required. Phase I trials examine the device in 15 – 30 patients, producing some basic data on how the device behaves in humans, rather than just in a lab. This allows some insight into how the changes affect the device's performance, without creating enough difficulty to dissuade manufacturers from updating devices with the newest technology that could benefit patients. Also, 23% of Denmark's clinical trials (for medical devices and pharmaceuticals) currently include 10 or fewer patients (Sundhedsstyrelsen, 2013), so requiring a minimum number of patients would improve the robustness of the trials that are already conducted. Ideally, the results of all clinical trials would be added to EUDAMED, which would provide a resource for doctors and patients with enough information for them to be able to compare different devices and find more information on any devices they may be considering.

To account for industry concerns about regulating devices based on overly broad categories, **there should be some flexibility built into this system**. First, the trial phases described above are the minimum requirement for new or updated devices. For devices considered particularly risky, such as those that require a complex surgery to implant, notified bodies would retain the ability to request more data, either from more trial subjects or a longer

trial period. With the changes to notified bodies outlined in the next finding, this system should be strong enough to obtain an appropriate level of testing for any device before approval. Additionally, **competent authorities could grant exemptions from clinical trials in extraordinary cases**. For example, a patient whose life could be saved by a device still going through clinical trials could apply to use the device anyway. A manufacturer designing a device to treat a very rare condition, from which too few people suffer to run a clinical trial, could apply to produce the device without running a clinical trial at all.

Finding #5: There are too many notified bodies and they vary too widely in their standards for device approval.

As mentioned in the background chapter, there are several problems with the current regulatory system's notified bodies, private companies that approve certain types of medical devices. A problem brought up time and again in our interviews was the number of notified bodies – there are currently about 70 in the EU, and this is too many. Lene Laursen of Medicoindustrien said that "We think there are too many of them [notified bodies] and that some of them are of a poor quality." Further, the standards for device approval vary widely among the different notified bodies. As Arne Mølgaard stated, "some notified bodies have had a very easy approval process." And Lene Laursen: "They are really the weak link in this whole area."

According to European Parliament member Christel Schaldemose, "One [notified body] used two hours and some used two weeks to approve the same product… They [notified bodies] have this different level of how they check new products." Dr. Lose gave us an example of a study done by the BMJ (Cohen, October 2012), in which a fake implant and fake documentation were set up, intentionally designed to have serious flaws which any notified body should have been able to detect. This was submitted for approval to 14 notified bodies, and in fact 10 of them approved the faulty device.

Another problem stems from the disparity in the number of notified bodies in each EU member country. Denmark has one notified body; Germany has 13. As mentioned in chapter 2, each country has a competent authority which supervises the notified bodies in its country. Of course, it is much easier to supervise one notified body than to supervise 13, but Peter Bøge brought our attention to another subtler issue. Consider a small country, which has one notified body. The country's notified body will be inspected by its competent authority. But the country

wants to keep the business run by its only notified body, so if there is a problem with the notified body, it may well go unaddressed. As Bøge put it, "If you can't trust the authorities then you can't trust the notified bodies."

With this amount of notified bodies in the EU available to approve devices, companies can "shop around" for the notified body with the easiest approval process, according to Kristine Rasmussen of Sundhedsstyrelsen. Schaldemose agrees, saying "If stopped by one notified body, they [companies] can go to another once the device is not approved." Laursen assured us that in her experience companies do not do this, preferring instead to go to a notified body with high standards so that they can be assured their products are appropriately safe and effective. However, the current system still allows for the possibility of an unscrupulous company immediately applying to another, less stringent notified body for approval after failing to get approval from a stricter one. There are also no restrictions on national companies going through the approval process with notified bodies based in other countries.

Finally, there remains a potential conflict of interest: notified bodies are for-profit and are funded by review fees from manufacturers (which can be quite large). As a result some notified bodies might be motivated to compete with one another for business – lowering their standards for approval in the hope that more companies will work with them to get their devices approved. "The system has created that the Notified Body dependents on paying manufacturers. Due to this system an independent examination of the manufacturer and his products is not always an easy task of the involved personal of the Notified Body. The satisfaction of the client/manufacturer is too often based upon getting a CE certificate. Making profit is a need for the Notified Body to survive," (Ruys, 2008). To fix this, as Peter Bøge mentioned, there needs to be an authority to "push them from the other end" to make sure that they hold manufacturers to a high standard. In some cases, the competent authority is not enough.

At first glance, it might appear that a possible solution is to centralize everything, and introduce a kind of "EU notified body" which would be responsible for approving devices from all EU member countries. While this would solve problems of disparate standards and conflicts of interest (with only one notified body, there is no competition), it is impossible for the time being. According to Christel Schaldemose, "I don't believe we will get a European notified body at this stage. The industry and many member states did not like it and they played on the fear of this big slow bureaucratic EU system, and I don't think that will be possible. And I think if we

got a more clear EU system we could make more progress." Indeed, the industry representatives we spoke with find the current system of multiple notified bodies "brilliant" (P. Bøge, personal communication, March 30, 2015) in some ways, much more effective than that of the US in getting medical devices onto the market quickly.

Thus, in the interest of feasibility, we recommend instead, based on our interviews, that **the number of notified bodies in the EU should be reduced**. Dr. Lose said "One thing would be… to reduce the number, and improve the quality" and Peter Bøge thinks that perhaps some of the notified bodies ought to go out of business to "set the example." This would address the problem of companies shopping around for notified bodies to some extent, and combined with our second recommendation below, would address the other issues described above.

We also propose introducing a centralized EU overseeing body, not to approve devices, but to directly investigate notified bodies and to make sure the competent authorities are maintaining high standards for the notified bodies in their respective countries. As Arne Mølgaard pointed out, "Everybody agrees that someone from the EU level has to watch them." Having an EU-level oversight in place would make the standards for device approval more consistent between countries and between notified bodies, and lead to making the approval process "more objective," which Gunnar Lose suggested. Raising the standards for device approval among all notified bodies would also help to eliminate conflict of interest; a notified body could no longer rely on being the only one in its country and lowering its standards to get more business if an EU overseeing body were also investigating it.

These recommendations are not substantially different from those being put forward in the European Parliament as of this writing. In fact, Christel Schaldemose said "To reduce the number of notified bodies is in the bill right now, as well as more control." We believe these issues must be resolved to make the medical device approval process safer, which is critical to ensure medical device safety.

Finding #6: Standards are an integral and necessary part of the medical device approval process, but are currently written primarily by industry representatives.

Standards play an important role in the EU medical device approval system because they have a few advantages over direct legislation for every individual medical device. First, they can

be updated quickly. For example, the International Organization for Standardization (ISO) imposes a time limit of two years from when a standard is proposed to when it must be finalized and passed, or the entire process for that standard must restart. Hence, standards committees have an incentive to work quickly, whereas legislation takes much longer to pass. The current proposals for medical device regulation changes have been in the European Parliament for several years already, and a final vote has been postponed multiple times. The accelerated timetable means that standards more closely reflect the state of the art than legislation possibly can. Different standards can also be created for each individual product while legislation remains broadly applicable. For example, if the safe electrical current for an X-ray machine and a pacemaker is different, the legislation might simply state that the current for all devices must be at a safe level. Manufacturers can then consult the standard to see what this level is, rather than conducting tests to determine what current is safe for patients.

However, there are a few problems with standards as they currently exist. Standards are constructed primarily by industry representatives. Lene Laursen emphasized that these representatives have no desire to make weak standards: their companies' reputations depend on creating good products that help patients. However, she still recognized the lack of other people on standards committees as a "weakness." Peter Bøge explained that this situation is due primarily to financial concerns. Sending representatives to standards committees requires money, at the very least for lost productivity while employees work on the standards instead of other matters. Manufacturers have the money for this and are willing to spend their money to have a say in the standards, while other groups lack the necessary money or desire to contribute to standards. Bøge stated that Denmark has "decentralized the health care system more and more…no one can afford to pay [doctors for work on standards] in the small units." The same problem applies for patients, who are only organized at an individual level, and regulatory agencies simply choose to spend their funds elsewhere.

Unfortunately, this has led to skepticism at a governmental level regarding many of the standards. According to Bøge and Laursen, the EC has recently begun questioning whether the harmonized standards are actually sufficient to show compliance with the essential requirements. As Bøge says, for the authorities, standards are "one big black box… Why should they trust it?" This doubt about whether standards will stay harmonized has created a great deal of uncertainty for manufacturers. Of particular concern is the risk management standard. Laursen stated that

were this standard to fall, it would be nearly impossible for manufacturers to show that the process underlying their design and manufacturing is appropriate. These doubts about whether products designed based on currently acceptable standards will be approved later creates a huge business risk. Additionally, from the regulatory standpoint, the loss of concrete standards would add a great deal of extra work and subjectivity to the approval process.

One way to improve these problems would be to **diversify representation on standards committees**. Realistically, particularly in countries like Denmark with a public health care system, the funding for this would need to be provided by the government. In fact, Bøge and Laursen both criticized the current lack of funding for this purpose. In the end, though, it would be a worthwhile investment. The inclusion of doctors or other non-industry experts could provide an outside perspective that would be useful in crafting objectively better standards, while patients could offer up more information on what features would be most useful or worrisome for the people on whom the devices will be used. While regulators might not have as much to offer in creating the standards, their inclusion would allow them to place more trust in standards, adding stability and confidence to medical device design. In fact, this is the approach currently taken by the FDA, which, according to Bøge, has been sending representatives to standards committees and increasingly making use of standards over the past 20 years. Finn Andersen from UL said that the US and EU use many of the same standards, which demonstrates that the standards themselves are acceptable, but regulator involvement is required to develop trust.

Additionally, **requirements on standards could be loosened to allow the use of any internationally accepted standard, whether harmonized or not**. Peter Bøge told us that all standards "internationally recognize what everyone thinks is safe." Therefore, notified bodies should be able to determine the safety of a device based on its use of any widely accepted standard. This would reduce uncertainty regarding the validity of standards and provide guidance on the design of certain aspects of a device without requiring extensive testing that could place test participants at risk of harm and still miss some problems.

Finding #7: The relationships between medical device manufacturers and doctors present a conflict of interest.

Across the European Union, many doctors are benefiting economically from medical device manufacturers for promoting and using their devices. Dr. Gunnar Lose, who has been in

practice for many years, is concerned with the freedom that companies have to interact with doctors. He cites a specific example with a French doctor who had a patent for a device and then had a relationship with the manufacturer where he promoted his device through workshops put on by the company. Against his ethical and occupational obligation to remain unbiased, he used his status as a doctor and expert to promote his device to other doctors and received compensation and gifts for promoting the device. This is specifically against European law but as there is no enforcement, no one talks about the blatant conflict of interest. European Parliament member Christel Schaldemose, when asked what her wish list for medical device legislation was, stated that she wants "stronger control between doctors and medical device companies" (C. Schaldemose, personal communication, April 10, 2015).

Conflict of interest can be detrimental to ensuring patient safety as it runs the risk of doctors putting their own financial interests above providing the best care to their patients. When companies are able to have relationships with doctors that are based on pecuniary interests, there is no way to know if doctors are being influenced to prefer a specific product not because of its effectiveness, but because of the money they can earn.

The Danish competent authority saw the danger of allowing the conflict of interest and passed legislation to remove any conflict of interest, similar to the steps taken for pharmaceutical companies and doctors. We believe this legislation will be effective in Denmark but there is no comparable legislation in the EU as whole. Morten Dahl Nielsen outlined the new legislation during our interview. In October 2014 a new executive order on advertising of medical devices was published and it addresses economic advantages for health professionals. The new executive order entered into force on 1 November 2014. This executive order on advertising of medical devices states (as a main rule) that economic advantages must not be offered or given to health professionals for advertising purposes or otherwise to promote the sale of medical devices, unless it is an economic advantage covered by a specific exception in the executive order (M. Dahl Nielsen, personal communication, April 13, 2015). The competent authority extensively outlined which types of relationships between companies and doctors were allowed in an effort to protect the public health. The act limits gifts from companies to doctors to be no more than DKK 300 and can only be items for the office, such as pens, mouse pads, or calendars. Manufacturers cannot give doctors free devices to keep; it can only be in the form of lending for demonstration purposes and must be returned after a short period of time. Companies are no

longer allowed to pay for extravagant dinners or events for doctors; it is strictly limited in extravagance and can only be related to medical devices or professional information.

To enforce the new legislation, the Danish competent authority requires that doctors report to Sundhedsstyrelsen if they receive payment from medical device companies for participating in professional activities. This information is then posted on the competent authority's website so that it is transparent. All health professionals also must "apply for authorization or notify their affiliation with a medical device company established in Denmark:" this information will also be made public. Health professionals must notify the competent authority of the payment they receive for teaching, researching, and participating in clinical investigations if under DKK 200,000 and if they are to receive more than that, they must receive permission from the competent authority. To eliminate conflicts of interest, Christel Schaldemose believes "doctors' decisions should only be based on need and effectiveness and not a doctor's financial interest" (C. Schaldemose, personal communication, April 10, 2015).

We recommend expanding the Danish legislation regarding advertising of medical devices to all of the European Union. Patient safety should take precedence over economic advantages for medical professionals. On an EU level, legislation is needed to prevent medical professionals from receiving financial benefits from medical device manufacturers including gifts and compensation for promoting devices. The links between doctors and manufacturers should not be anything more than informational regarding devices, procedures, and treatments.

Project Conclusion

In the end, our project developed a comprehensive set of recommendations for changes to medical device regulation. For pre-market changes, we recommend using standards written by a diverse group of stakeholders and requiring some type of clinical trial involving humans for all devices. The data from these trials should be closely examined by one of the reduced number of notified bodies, overseen by a European Union-wide auditing organization. Once devices are on the market, information about them should be easily accessible and provided to all patients by their doctor before they undergo any serious procedure. Doctors should have enough information to choose the best device, and should not be advertised to by manufacturers in a way that might compromise this decision. After the procedure, they should report any immediate or long-term complications to their country's competent authority using an anonymous form, and this

information should be made publicly available to help other patients and doctors make future decisions. A summary of the complete recommendations can be found in Figure 4.5.

These findings and recommendations will be used by FBR's senior health officer, Sine Jensen, in her interactions with other health professionals to provide evidence for regulatory changes to improve patient safety. The recommendations also account for the industry perspective both to allow for continued innovation that could help patients, and to increase the feasibility of these recommendations being incorporated into new regulations. While some of our recommendations mirror parts of the proposals currently in the European Parliament, others are new ideas that could potentially improve the proposals. Even if they are not included in this revision of the directives, they offer interesting possibilities for the future that could be looked into more closely by the EU's governing bodies.

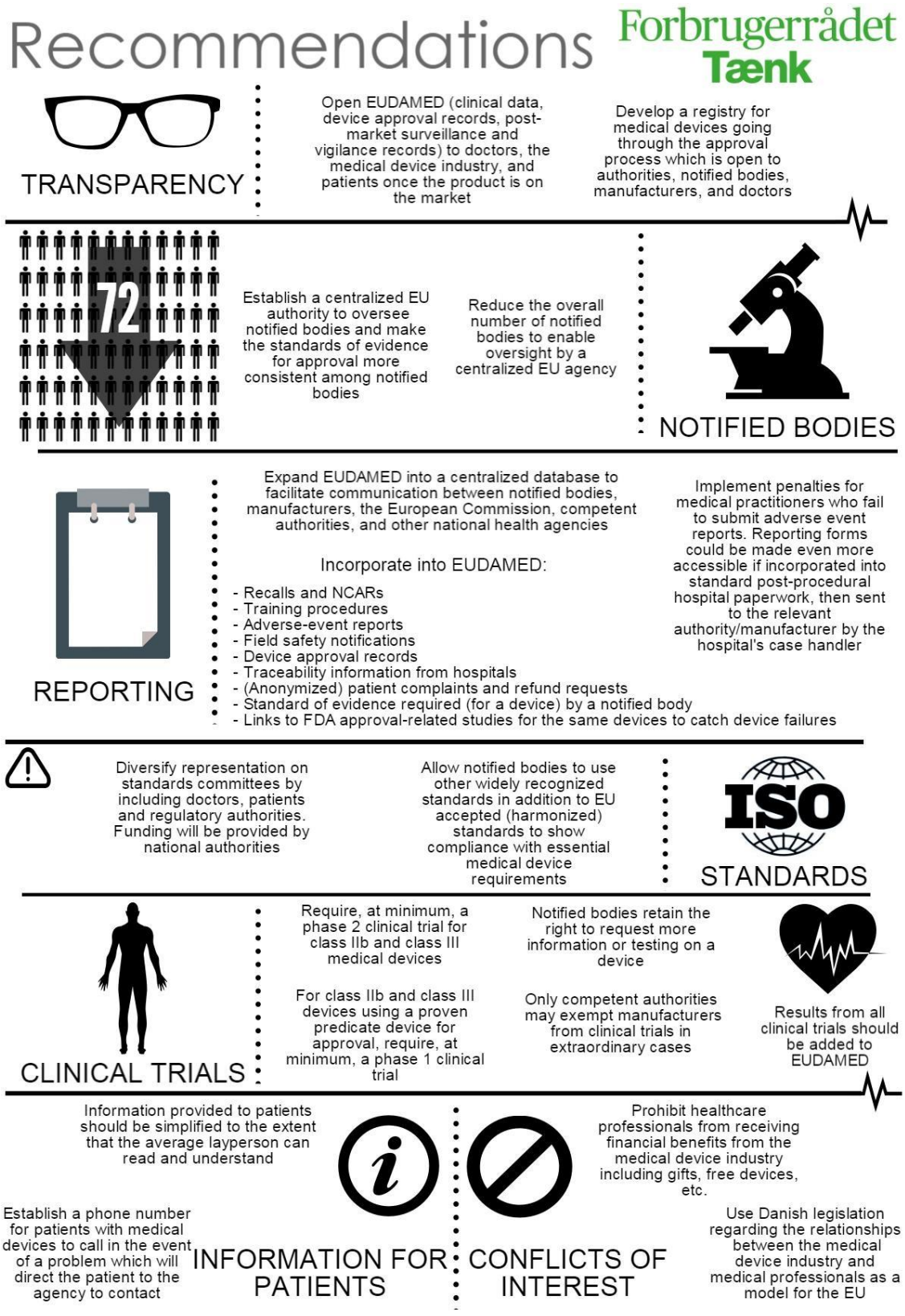

Figure 4.5 Recommendations Chart (Sam Jacobs, 2015)

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Appendix A: Survey

Part I: Original Danish Questions

Preamble

De første spørgsmål handler om oplysninger om dig selv. De er vigtige for at vi kan sikre at undersøgelsen er repræsentativ.

Survey

1. Hvad er dit køn?
    a) Kvinde
    b) Mand

2. Hvor gammel er du?
    a) Under 25 år
    b) 25-35 år
    c) 36-49 år
    d) 50-60 år
    e) Over 60 år

3. I hvilken landsdel har du din bopæl?
    a) Hovedstaden
    b) Sjælland
    c) Syddanmark
    d) Midtjylland
    e) Nordjylland
    f) Bornholm

4. Hvad er din højest opnåede uddannelse?
    a) Folkeskole, mellemskole, realeksamen eller lignende grundskole
    b) Erhvervsfalig uddannelse (f.eks. bager, tømrer, frisør, butiks- eller kontorassistent)
    c) Almen- eller erhvervsfaglig gymnasial uddannelse (f.eks. HTX, gymnasium, HHX, HF eller HH)
    d) Kort videregående erhvervsakademiuddannelse (f.eks. datamatiker, multimediedesigner, politi, forsvar eller laborant)
    e) Mellemlang videregående uddannelse (f.eks. diplomingeniør, sygeplejerske, folkeskolelærer eller bachelorgrad)
    f) Lang videregående uddannelse (f.eks. master, kandidat, ph.d. fra universitet, handelshøjskole eller tilsvarende)
    g) Anden uddannelse end de nævnte

5. Har du hjemmeboende børn under 18 år?
    a) Ja
    b) Nej

De følgende spørgsmål omhandler medicinsk udstyr. Medicinsk udstyr er produkter, der anvendes til at diagnosticere, forebygge, lindre eller behandle sygdomme, handicap, skader m.m. Det kan f.eks. være implantater, blodtryksmålere, plastre, spiraler, sonder og slanger osv. Medicinsk udstyr er ikke medicin og lægemidler.

6. Sidste gang, du havde kontakt med sundhedsvæsenet, blev der så anvendt medicinsk udstyr?
    a) Ja
    b) Nej
    c) Ved ikke

7. Blev du informeret om sikkerheden ved det udstyr, der blev anvendt?
    a) Ja, jeg fik meget information
    b) Ja, jeg fik noget information
    c) Ja, jeg fig lidt information
    d) Nej, jeg fik ingen information
    e) Ved ikke

8. I hvor høj grad stoler du på, at din læge/dit hospital vælger det rigtige medicinske udstyr til dig?
    a) I meget lav grad
    b) I lav grad
    c) Både og
    d) I høj grad
    e) I meget høj grad

9. Hvilke af følgende steder tror du at kontrollen af medicinsk udstyr før det kommer på markedet er størst?
    a) Japan
    b) EU
    c) USA

10. Har du på noget tidspunkt fået indopereret et implantat (f.eks. knæ, hofte, hjerteklap, brystprotese eller andet)?
    a) Ja
    b) Nej
    c) Ved ikke

11. Kunne du tænke dig at svare på flere uddybende spørgsmål angående medicinsk udstyr, f.eks. i form af et interview?
    a) Ja
    b) Nej

12. Tak fordi, at vi må kontakte dig med flere spørgsmål på et senere tidspunkt. På hvilken email-adresse kan vi kontakte dig?

    _____

Part II: English Translation of the Questions

Preamble

The first questions ask for information about yourself. They are important for us to ensure that the survey is representative.

Survey

1. What is your gender?
    a) Female
    b) Male

2. How old are you?
    a) Under 25 years
    b) 25-35 years
    c) 36-49 years
    d) 50-60 years
    e) Over 60 years

3. What region do you live in?
    a) Capital
    b) Zealand
    c) South Denmark
    d) Mid Jutland
    e) Northern Jutland
    f) Bornholm

4. What is your highest level of education?
    a) Ordinary school (up to 9th grade)
    b) Vocational (e.g. training, apprenticeship)
    c) Trade school/high school
    d) Short-term education (e.g. policeman, defense, etc.)
    e) Medium-term education (e.g. nurses, teachers, Bachelor's degree)
    f) Long-term education (e.g. Master's, PhD)
    g) Other education

5. Do you have any children under 18 living at home?
    a) Yes
    b) No

The following questions concern medical devices. Medical devices are products used to diagnose, prevent, alleviate or treat illnesses, injuries, etc. Some examples are implants, sphygmomanometers, patches, coils, probes and hoses etc.
Medical devices are not drugs or pharmaceuticals.

6. The last time you were in contact with a health service, was any medical device used?
    a) Yes
    b) No
    c) Don't know

7. Were you informed about the safety of the equipment used?
    a) Yes, I got a lot of information
    b) Yes, I got some information
    c) Yes, I got a little information
    d) No, I got no information
    e) Don't know

8. How much do you trust your doctor/your hospital to choose the right medical device for you?
    a) Very much
    b) Much
    c) Enough
    d) Little
    e) Very little

9. Which of the following places do you think the control of medical devices is highest, before the products come to market?
    a) Japan
    b) EU
    c) USA

10. Have you at any time had an operation where you have had an implant inserted? (e.g. knee, hip, heart valve, breast implants or anything else)?
    a) Yes
    b) No
    c) Don't know

11. Would you like to answer further questions about medical devices, for example in an interview?
    a) Yes
    b) No

12. Thank you. If we may contact you with more questions later, on which email can we contact you?

    _____

Appendix B: Interview Questions

Questions for Anonymous Survey Respondent

1. How much did your doctor tell you about the implant before your procedure?
2. Did you receive any information on the benefits and risks of the implant? How much?
3. Have you received information about the Patient Compensation Association or the Patient Complaint Agency? (if so, at what point did you receive this information?)
4. Was the amount of information about the implant enough to make you feel comfortable with the procedure?
5. What do you feel you have the right to know about the implant?
6. Do you think patients have a right to this information regardless if they were to use it?
7. Do you have any thoughts or opinions you would like to share with us?
8. Do you have any questions for us?

Questions for Finn Andersen (Underwriters Laboratories)

1. Can you tell us a little more about your role at UL?
2. Why do medical device companies in the EU come to you to test their devices?
3. What do you do for them?
4. Do most European medical device companies work with companies like UL to perform testing?
5. What are differences in the information required by the FDA versus a typical notified body regarding medical devices undergoing clinical trials?
6. What kind of information are notified bodies looking for with high risk devices (i.e. implant)?
7. Are there any other non-profits like UL in the world?
8. Do you think there should be more similar requirements between the FDA and the EU?
9. Do you have any questions for us?

Questions for Martin Bommersholdt (National Agency for Patients' Rights and Complaints, Senior Patient Safety Officer)

1. Could you tell us more about your role at the Agency for Patient's Rights and Complaints?
2. How do you follow up on complaints? With whom?
3. Have you found this to be an effective framework for filing and addressing complaints? Are there any specific changes you would make?
4. Are the majority of the complaints you receive attributed to user-error, or device failure?
5. Are Danish patients usually well informed? Do the patients know enough? What is the standard practice for informed consent?
6. Do you think the number of complaints you receive accurately reflects how many problems patients experience? Do you think that the majority of Danish patients know this complaint system is in place?

Questions for Peter Bøge (Novo Nordisk, Standards)

1. We would like to know more about your role and how you work with standards from the industry perspective and the standardization perspective.
2. Which aspects of the medical device manufacturing process are covered by standards?
3. How are standards enforced? What level of flexibility do companies have in deciding which standards to adopt or whether to adopt particular standards?
4. How are standards decided upon? Is there a different process involved depending on the standard? Who drafts the standards?
5. Is there anything you would change about the current standards you directly work with? What components would you keep? What is your opinion on the current process of how standards are developed and enforced?

Questions for Peter Jakobsen and Birgitte Frost (Patient Compensation Association)

1. Could you tell us more about your role at the Patient Compensation Association?
2. How does the process for refunds work?
3. Where does the money for compensation come from (e.g. from government, doctors, or companies via insurance, etc)?
4. How are refund requests prioritized and evaluated? What are the guiding principles in the decision making process?
5. How are requests stored and analyzed? Is the information publicly available?
6. In your experience, do more problems arise from inherent problems with devices or from user error? Which types of devices tend to have more problems associated with them?
7. If you have a concern with the safety of the device is there a process you follow to alert the proper authorities (for instance the DKMA) or the manufacturer?
8. Do you think that the number of complaints you receive accurately reflects how many problems patients experience? Do you think that the majority of Danish patients know this compensation system is in place?
9. Have you found this to be an effective framework for addressing the problems and complications that patients may encounter?
10. What works well in the current system? Are there any aspects of it that could be changed or improved?

Questions for Lene Laursen (Medicoindustrien, Vice-Director)

1. We would like to hear more about your role at Medicoindustrien.
2. What is your opinion on the role of standards in the medical device approval process? Would you prefer a greater emphasis on standards or a greater emphasis on legislation in the future? Would you prefer more standards be harmonized or does it not matter?
3. Do you believe there is sufficient oversight surrounding the notified bodies?
4. How large do you think the difference in ease-of-approval is between different notified bodies?
5. What changes to the regulatory system would you make?

6. What elements, if any, do you think are good about the US medical device regulatory system? What is better in the EU system? What are the advantages of other systems (e.g. Japan)? What improvements could be made to each system?
7. Have there been efforts by the industry to change any particular medical device regulations? If so, which ones? Which regulations would the medical device industry in general prefer not be changed?
8. What is your opinion on the current proposals for change that have been made in the EU?

Questions for Gunnar Lose (Professor and practicing gynecologist at Herlev Hospital)

1. Do you, when practicing medicine, have confidence in the medical devices you are working with? Have you encountered any complications due to medical device malfunction?
2. Do you have any experience working with transvaginal mesh? If so, what have those experiences been?
3. Based on your knowledge of the transvaginal mesh and its recall, where in the approval process do you believe that the problems with the mesh should have been caught? Do you know if there are any measures in place to fix this?
4. Sine mentioned that you picked up on the fact that when a device is recalled, there is no investigation performed upon the predicate devices that were used as presumably safe, similar devices, for the recalled device. What's the reason behind this? What are your opinions on this issue?
5. What are your thoughts on the device complication reporting process? What do you think could help motivate doctors to report complications more often?
6. Do you know how medical devices are chosen by hospitals to be used in patients? What considerations are made (e.g. safety, efficacy, ease of use, price)? Do doctors have the ability to choose devices, or are most decisions made at the hospital level?
7. What level of interest do the majority of your patients show in the medical devices that will be involved in their own procedures? What aspects of a procedure do you think patients tend to be most concerned about? Do patients ever express concern over the reliability or safety of the medical devices involved?
8. What are some specific changes to medical device regulation you would like to see and why?
9. Which components do you strongly feel should be retained?
10. How do you think we could best effect change in the regulatory system?

Questions for Arne Mølgaard (Cook Medical, Director of Research)

1. Is there one notified body that Cook Medical uses for approval of all devices intended for European markets?
2. How much does it typically cost to get the CE mark on a medical device?
3. How often does Cook Medical conduct clinical trials when they are not mandated by a notified body?

4. Who makes sure that your medical devices are in accordance with ISO-13485? Does the company comply to that standard and check that it is compliant before reaching out to a notified body?
5. From an industry standpoint, have you noticed any gaps in ISO-13485?
6. Can you walk us through what happens between Cook Medical and the notified body once all documentation has been handed over?
7. How do you think the EU's regulatory has changed over time since you started working at Cook Medical?
8. Are there any particular changes you can think of that would make the EU's medical device policies more effective?

Questions for Morten Dahl Nielsen (Sundhedsstyrelsen, advertising)

1. Are relationships between doctors and medical device manufacturers regulated? How?
2. What kind of advertising do doctors/hospitals see from medical device manufacturers?
3. Do you know how medical device recalls are publicized? If you do, how aware is the public of these recalls?
4. Are there any recommendations that you would make to improve policies surrounding the promotion of medical devices in the EU?

Questions for Kristine Rasmussen, Inger Kühne, and Neel Larsen (Sundhedsstyrelsen)

1. Could you tell us a little about your role at the DKMA?
2. Do you have access to EUDAMED? Who else/does have access? What information regarding recalls and device complaints is released to the public? How is the information released? Why is this database closed to the public?
3. Are competent authorities able to recall products if they are shown to be unsafe? How often is it left up to the manufacturer? If so, what is the process for recalls?
4. Do you think there is an effective delegation of authority between the EU and nation states regarding medical device regulation? How has this been changing as of late?
5. Does the DKMA have any methods to ensure that Danish doctors report adverse events?
6. Do you think adapting standards to prioritize patient safety and keep up to date with emerging technologies is the most effective way of amending the EU's medical device regulations?
7. In which circumstances might you reject a company's application to have a clinical trial?
8. Do you believe that notified bodies should require medical device manufacturers to run more clinical trials, to provide more suitable evidence?
9. How do you think the burden of proof in the EU compares to that in the US? Do you think it is substantial enough to ensure patient safety?
10. Do you believe there is sufficient oversight surrounding the notified bodies?
11. How are notified bodies supervised and regulated? Are random audits ever performed?
12. How large do you think the biggest difference in ease-of-approval is between different notified bodies?
13. What is the extent of the involvement of the Ethics Committee?

14. Is there room for interpretation of directives between national authorities? Do you think Denmark implements the directives differently from other countries?
15. What are some specific changes to medical device regulation you would like to see and why?
16. Which components do you strongly feel should be retained?

Questions for Christel Schaldemose (European Parliament)

1. Suppose there is a change that would improve safety supported by only one group or a few groups. How would this be lobbied through; what is the process?
2. Of the current medical device legislation proposals being debated, what changes did you propose?
3. There have been proposals to change medical device regulations since 2012? What has prevented these passing through parliament so far?
4. What forces in the European Parliament provide the opposition to changing medical device regulations? What forces have been working to get the new regulations passed?
5. Of the proposals put forward to the EU so far, which do you think are likely to be actually accepted? Why? What about the ones that are less likely to pass?
6. How do you think the approval of combination pharmaceutical/medical device products (such as a drug eluting stent) should be approached?
7. What is your wish list for medical device legislation? If you knew it would be passed, what would you include in a proposal for changes?
8. Do you know how likely the other countries are to measure up to these standards and follow the directives?
9. This is the direction we see our recommendations going:
    1. Diversify representation in standards committees (i.e. not just industry, but government and NGO representation as well).
    2. Increase transparency, for example allow more access to EUDAMED.
    3. More clinical trials required for medical device approval.
    4. Accountability for not registering complications.
    5. More information (clinical or other) presented to patients pre-procedure.
    6. Notified Bodies:
        a. More oversight of notified bodies.
        b. Consistency in how they approve medical devices.
        c. Normalize burden of proof between notified bodies.

    Are these feasible?
10. What are your views on EUDAMED? Should it be open to the public?
11. Doctors can choose whatever project they prefer for any patient; can we do anything in legislation to ensure that it's not up to one single doctor to choose?